Facultad de Ciencias

Departamento de Química Orgánica

Pd-Catalyzed Borylative Cyclization Reactions of Polyunsaturated Compounds. Synthesis of Alkyl- and Allylboronates

TESIS DOCTORAL

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Facultad de Ciencias

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PRÓLOGO

Esta memoria recoge el trabajo y los resultados obtenidos a lo largo de la realización de la Tesis Doctoral. El manuscrito incluye una *Introducción* que consta de tres apartados; el primero de ellos describe la naturaleza y el comportamiento de los compuestos de boro, y más concretamente de los derivados de los ácidos borónicos (ésteres), haciendo especial mención a su clasificación, propiedades, métodos de preparación y reacciones en las que se ven involucrados. Por otra parte, en un segundo apartado se tratan las reacciones de ciclación de eninos catalizadas por metales de transición, centrándose en los aspectos mecanísticos de las mismas y el desarrollo de este tipo de ciclaciones mediante procesos tipo tándem o en cascada. Por último, en la tercera parte, se recogen los procesos análogos de ciclación en la química de aleninos y enalenos.

El apartado de *Resultados y discusión* se divide en tres secciones principales donde se exponen los resultados obtenidos para la reacción de ciclación borilativa de compuestos poliinsaturados. En un primer apartado se recoge el desarrollo de la nueva reacción y la síntesis de alquilboronatos partiendo de eninos como sustratos iniciales. En el segundo, a su vez dividido en dos partes, se expone la síntesis de alil- y alquilboronatos bicíclicos por ciclación borilación en cascada de diferentes tipos de endiinos. Por último, en el tercer apartado, se recogen los resultados obtenidos para la preparación de alil- y alquilboronatos cuando se emplean aleninos y enalenos como sustratos de partida, haciendo especial mención a la diferente reactividad de las instauraciones. Hay que destacar, que en todos los apartados, se recogen las posibles transformaciones de los boronatos obtenidos como punto de partida para la síntesis de otros compuestos. Además de recoger los resultados y los datos más relevantes del trabajo, se presentan las diferentes propuestas mecanísticas, fruto de la investigación tanto en el campo experimental como en el computacional, que han proporcionado un conocimiento más profundo sobre el transcurso de la reacción desarrollada.

El trabajo de investigación recogido en la primera sección permitió la consecución del Diploma de Estudios Avanzados y fue realizado con la colaboración de Verónica López Carrillo y de Raquel Simancas. En el trabajo recopilado en la segunda parte de la segunda sección se contó con la colaboración de Rebeca Muñoz Rodríguez y en la tercera sección con Virtudes Pardo Rodríguez. En este último caso, parte de sus resultados han sido incluidos en esta memoria para dar más coherencia al trabajo.

Los estudios computacionales han sido realizados por los directores de este trabajo.

Hasta el momento de redactar esta memoria, el trabajo realizado a lo largo de los años de realización de esta Tesis Doctoral ha dado lugar a las siguientes publicaciones:

- *"Pd-Catalyzed Borylative Cyclization of 1,6-Enynes"*
  Juan Marco-Martínez, Verónica López-Carrillo, Elena Buñuel, Raquel Simancas, Diego J. Cárdenas. *J. Am. Chem. Soc.* **2007**, *129*, 1874-1875.

- *"Pd-Catalyzed Borylative Polycyclization of Enediynes to Allylboronates"*
  Juan Marco-Martínez, Elena Buñuel, Rebeca Muñoz-Rodríguez, Diego J. Cárdenas. *Org. Lett.* **2008**, *10*, 3619-3621.

- *"Pd-Catalyzed Borylative Cyclization of Allenynes and Enallenes"*
  Virtudes Pardo-Rodríguez, Juan Marco-Martínez, Elena Buñuel, Diego J. Cárdenas. *Org. Lett.* **2009**, *11*, 4548-4551.

RESUMEN

[†]La continua búsqueda de moléculas biológicamente activas es una de las áreas de investigación más extensas en la cual la química orgánica juega un papel fundamental. Dado que la mayoría de estas moléculas, incluso los productos naturales de uso comercial, se sintetizan en el laboratorio, existe una constante demanda de nuevos métodos para la construcción selectiva de enlaces C–C.

La mayoría de las nuevas reacciones de interés sintético que se vienen desarrollando durante los últimos años surgen de la química organometálica de los metales de transición. Las reacciones de acoplamiento de electrófilos orgánicos con compuestos organometálicos nucleófilos (de Mg, Zn, Al, Zr, Sn, Si, B) catalizadas por metales de transición han ampliado el arsenal de procesos sintéticamente útiles y se han convertido en herramientas de uso común a la hora de formar nuevos enlaces C–C.[1]

La reacción de este tipo que más se ha desarrollado recientemente es la de Suzuki (o Suzuki-Miyaura), que consiste en el acoplamiento de haluros o triflatos orgánicos como electrófilos y organoboranos como nucleófilos, y está catalizada por complejos de Pd y en algunos casos de Ni.[2] La reacción es aplicable a diversos nucleófilos de B (triorganoboranos, ácidos borónicos y boronatos; que pueden ser derivados de alquilo, alquenilo, alquinilo, arilo o heteroarilo). Desde su publicación en 1979, la síntesis y aplicación de ácidos borónicos y de sus derivados ha experimentado un crecimiento exponencial, situándose en la primera línea de los intermedios en síntesis orgánica.[3] Por tanto, el desarrollo de nuevos métodos para la preparación de derivados de B, especialmente ácidos borónicos, ésteres de ácidos borónicos y sales de trifluoroborato, es especialmente útil dada la potencial proyección de estos compuestos por su posible aplicación a este tipo de reacciones de acoplamiento y de formación de nuevos enlaces

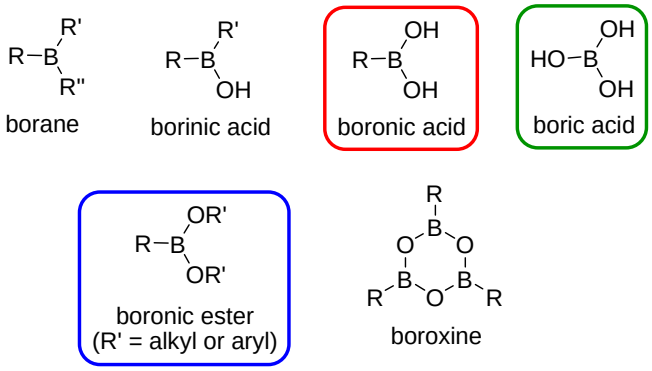
[†] En este resumen se ha respetado la numeración de los compuestos tal y como aparece en los capítulos siguientes. La numeración de las referencias bibliográficas es, sin embargo, independiente del resto de las secciones que componen esta memoria.

[1] *Metal-catalysed Cross-coupling Reactions*; de Meijere, A., Diederich, F., Eds.; Wiley-VCH: Weinheim, Germany, 2004.

[2] (a) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457-2483. (b) Suzuki, A. *J. Organomet. Chem.* **1999**, *576*, 147-168. (c) Miyaura, N. *Top. Curr. Chem.* **2002**, *219*, 11-59. (d) Kotha, S.; Lahiri, K.; Kashinath, D. *Tetrahedron* **2002**, *58*, 9633-9695. (e) Hassan, J.; Sévignon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 1359-1469. (f) Molander, G. A.; Ellis, N. *Acc. Chem. Res.* **2007,** *40*, 275-286. (g) Doucet, H. *Eur. J. Org. Chem.* **2008**, 2013-2030.

[3] *Boronic Acids*; D. G. Hall, Ed.; Wiley-VCH: Weinheim, Germany, 2005.

C–C. Además, otras muchas propiedades caracterizan a los compuestos de B, como pueden ser su suave caráter de ácido de Lewis que le aporta una atenuada reactividad y les hace fáciles de manipular, y su baja toxicidad debido a su degradación final a ácido bórico que los convierte en compuestos respetuosos con el medioambiente.



Existen un gran número de métodos descritos en la bibliografía para la preparación de boranos. Así, por ejemplo, se pueden enumerar la reacción de reactivos organometálicos (organolíticos y organomagnésicos) con boratos,[4] la transmetalación directa de haluros con compuestos bimetálicos de boro (B_2pin_2)[5] o de boranos con otros compuestos metálicos (silanos),[6] hidroboración de alquenos y alquinos,[7] y en los últimos años, bismetalación de compuestos insaturados[8] o borilación directa por activación de enlaces C–H.[9]

[4] (a) Matteson, D. S.; Peacock, K. *J. Org. Chem.* **1963**, *28*, 369-371. (b) Stürmer, R. *Angew., Chem., Int. Ed.* **1990**, *29*, 59-60. (c) Das, S.; Alexeev, V. L.; Sharma, A. C.; Geib, S. J.; Asher, S. A. *Tetrahedron Lett.* **2003**, *44*, 7719-7722.

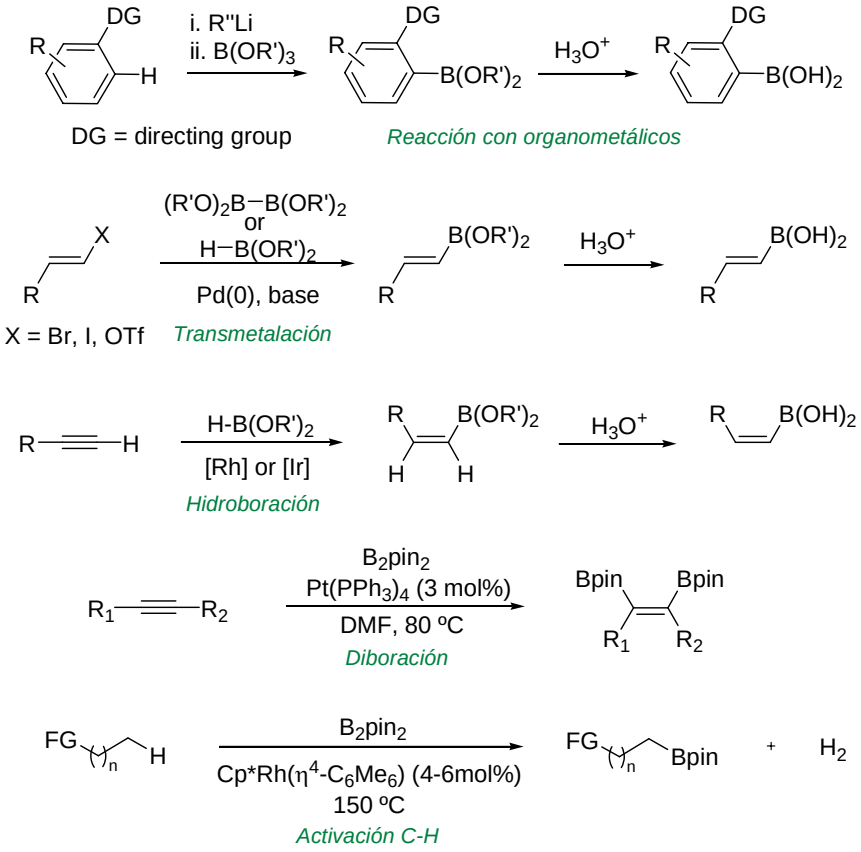
[5] Ishiyama, T.; Murata, M.; Miyaura, N. *J. Org. Chem.* **1995**, *60*, 7508-7510.

[6] Itami, K.; Kamei, T.; Yoshida, J.-I. *J. Am. Chem. Soc.* **2003**, *125*, 14670-14671.

[7] Beletskaya, I.; Pelter, A. *Tetrahedron Lett.* **1997**, *53*, 4957-5026.

[8] Diboración: (a) Marder, T. B.; Norman, N. C. *Top. Catal.* **1998**, *5*, 63-73. (b) Ishiyama, T.; Miyaura, N. *J. Organomet. Chem.* **2000**, *611*, 392-402. (c) Burks, H. E.; Liu, S.; Morken, J. P. *J. Am. Chem. Soc.* **2007**, *129*, 8766-8773. Borilsililación: (d) Onozawa, S.; Hatanaka, Y.; Tanaka, M. *Chem. Commun.* **1997**, 1229-1230. (e) Ohmura, T.; Taniguchi, H.; Suginome, M. *J. Am. Chem. Soc.* **2006**, *128*, 13682-13683. Borilestannilación: (f) Onozawa, S.; Hatanaka, Y.; Sakakura, T.; Shimada, S.; Tanaka, M. *Organometallics* **1996**, *16*, 5450-5452. (g) Onozawa, S.; Hatanaka, Y.; Tanaka, M. *Chem. Commun.* **1999**, 1863-1864.

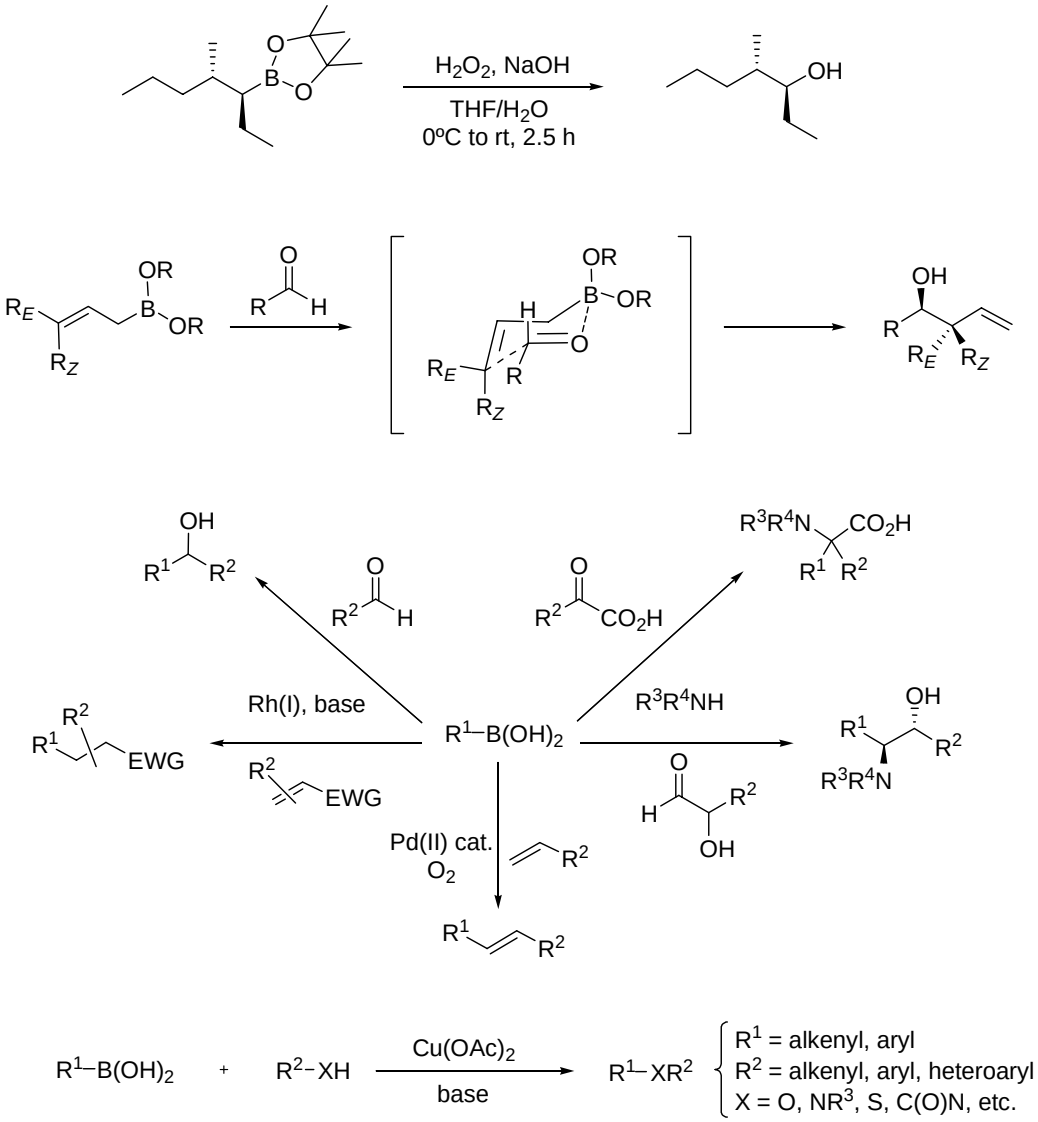
[9] For Re: (a) Waltz, K.M.; Hartwig, J. F. *Science* **1997**, *277*, 211-213. (b) Chen, H.; Hartwig, J. F. *Angew. Chem., Int. Ed.* **1999**, *38*, 3391-3393. For Rh: (c) Lawrence J. D.; Takahashi M.; Bae C.; Hartwig, J. F. *J. Am. Chem. Soc.* **2004**, *126*, 15334-15335. (d) Mkhalid, I. A. I.; Coupes, R. B.; Edes, S. N.; Coventry, D. N.; Souza, F. A. S.; Thomas, R. Ll.; Hall, J. J.; Bi, S.-W.; Lin, Z.; Marder, T. B. *Dalton Trans.* **2008**, 1055-1064. For Ru: (e) Murphy, J. M.; Lawrence J. D.; Kawamura, K.; Incarvito, C.; Hartwig, J. F. *J. Am. Chem. Soc.* **2006**, *128*, 13684-13685.



Este amplio arsenal de derivados de boro no sólo ha encontrado su aplicación en la reacción de Suzuki, sino que existen un gran número de reacciones, independientemente de su comportamiento como nucleófilos o electrófilos, que emplean esta serie de compuestos como intermedios para la obtención de otros grupos funcionales, como la oxidación a alcoholes,[10] la aminación,[11] o la halogenación;[12] y también la formación de enlaces C–C mediante otros procedimientos. Entre las reacciones más destacadas se encuentran, entre otras, la alilación de compuestos carbonílicos a partir de alilboronatos,[13] la adición no catalizada a iminas,[14] la adición a aldehídos[15] y alquenos[16]

[10] (a) Ainley, A. D.; Challenger, F. *J. Chem. Soc.* **1930**, 2171-2180. (b) Tripathy, P. B.; Matteson, D. S. *Synthesis* **1990**, 200-206.
[11] (a) Brown, H. C.; Kim, K.-W.; Cole, T. E.; Singaram, B. *J. Am. Chem. Soc.* **1986**, *108*, 6761-6764. (b) Prakash, G. K. S.; Panja, C.; Mathew, T.; Surampudi, V.; Petasis, N. A.; Olah, G. A. *Org. Lett.* **2004**, *6*, 2205-2207.
[12] (a) Brown, H. C.; De Lue, R. B. *Synthesis* **1976**, 114-116. (b) Szumigala, R. H., Jr.; Devine, P. N.; Gauthier, D. R., Jr.; Volante, R. P. *J. Org. Chem.* **2004**, *69*, 566-569.
[13] (a) Blais, J.; L'Honoré, A.; Soulié, J.; Cadiot, P. *J. Organomet. Chem.* **1974**, *78*, 323-337. (b) Denmark, S. E.; Almstead, N. G. *Modern Carbonyl Chemistry*; Otera, J., Ed.; Wiley-VCH: Weinheim, Germany, 2000, capítulos 10 y 11. (c) Kennedy, J. W. J.; Hall, D. G. *Angew. Chem., Int. Ed.* **2003**, *42*, 4732-4739. (d) Rauniyar, V.; Zhai, H.; Hall, D. G. *J. Am. Chem. Soc.* **2008**, *130*, 8481-8490.
[14] (a) Petasis, N. A.; Akritopolou, I. *Tetrahedron Lett.* **1993**, *34*, 583-586. (b) Sieber, J. D.; Liu, S.; Morken, J. P. *J. Am. Chem. Soc.* **2007**, *129*, 2214-2215.
[15] Sakai, M.; Ueda, M.; Miyaura, N. *Angew. Chem., Int. Ed.* **1998**, *37*, 3279-3281.
[16] Sakai, M.; Hayashi, H.; Miyaura, N. *Organometallics* **1997**, *16*, 4229-4231.

catalizada por Rh, el acoplamiento tipo Heck a alquenos[17] y alquinos,[18] o la formación de enlaces C–heteroátomo con nucleófilos heteroatómicos catalizada por Cu.[19]



Por otro lado, gran parte de las sustancias biológicamente activas que se encuentran en la naturaleza o que se sintetizan en la industria farmacéutica contienen ciclos carbonados o heterociclos como esqueletos básicos en su estructura. Para este fin, un gran número de reacciones de ciclación de especies poliinsaturadas y catalizadas por metales de transición han sido desarrolladas durante los últimos años. Estas

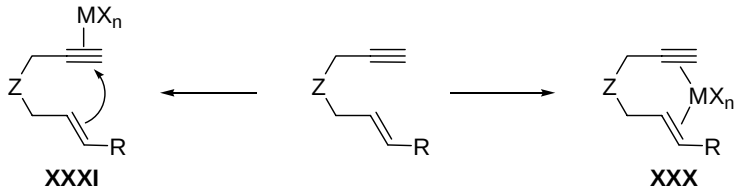
[17] For Rh: (a) Zou, G.; Wang, Z.; Zhu, J.; Tang, J. *Chem. Commun.* **2003**, 2438-2439. For Ru: (b) Farrington, E. J.; Brown, J. M.; Barnard, C. F. J.; Rowsell, E. *Angew. Chem.*, *Int. Ed.* **2002**, *41*, 169-171. For Ir: (c) Koike, T.; Du, X.; Sanada, T.; Danda, Y.; Mori, A. *Angew. Chem.*, *Int. Ed.* **2003**, *42*, 89-92.

[18] Zou, G.; Zhu, J.; Tang, J. *Tetrahedron Lett.* **2003**, *44*, 8709-9711.

[19] (a) Chan, D. M. T.; Monaco, K. L.; Wang, R.-P.; Winters, M. P. *Tetrahedron Lett.* **1998**, *39*, 2933-2936. (b) Ley, S. V.; Thomas, A. W. *Angew. Chem.*, *Int. Ed.* **2003**, *42*, 5400-5449.

metodologías han permitido la preparación de sistemas cíclicos con altos niveles de selectividad y de economía atómica, y en muchos de los casos su aplicabilidad a la industria debido a las suaves condiciones de reacción empleadas.

Entre los compuestos poliinsaturados más utilizados en química organometálica para este fin destacan los 1,6-eninos por su variada reactividad con diferentes catalizadores metálicos.[20] Dentro de las reacciones de ciclación que involucran esta serie de compuestos se pueden distinguir varios tipos en función de cómo se produzca la coordinación al enino. Si tanto el alqueno como el alquino se coordinan al metal se obtiene el complejo **XXX**, mientras que si sólo se produce la coordinación del triple enlace, se obtiene el complejo **XXXI**, que reacciona con el alqueno cómo nucleófilo.



Además, en función de los productos de cicloisomerización obtenidos, cabe clasificar estas reacciones en dos tipos: (a) reacciones de tipo Alder-énica,[20c] y (b) reacciones de transposición de esqueleto.[21]

Dentro de las reacciones de tipo Alder-énica, se pueden distinguir tres tipos de mecanismo:

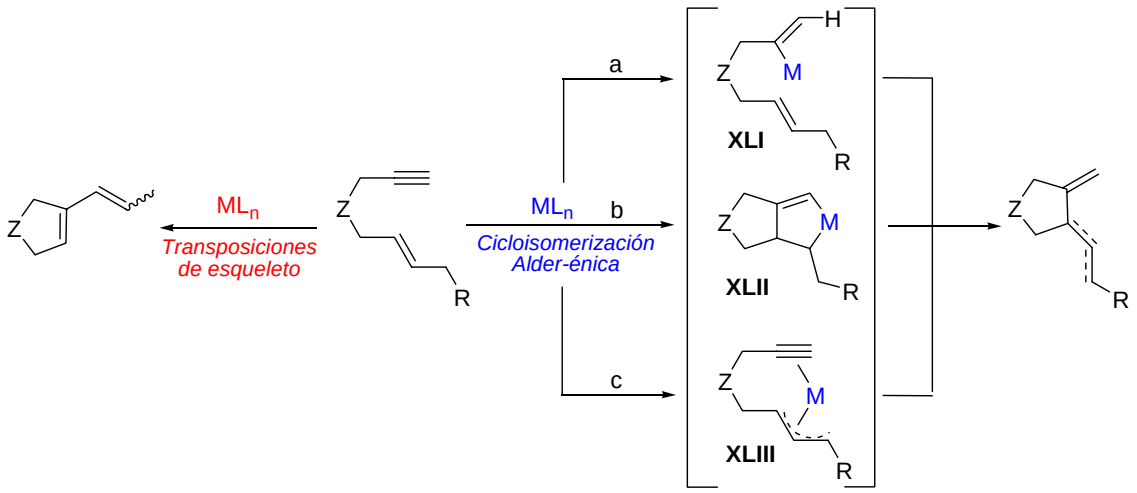
(a) Hidrometalación del alquino con especies M–H para dar complejos intermedios tipo vinilmetal **XLI**.

(b) Ciclometalación oxidante por coordinación simultánea a ambas instauraciones formando así un complejo de metalaciclopenteno **XLII**.

(c) Formación de un complejo de π-alilo **XLII** en el doble enlace que puede reaccionar posteriormente con el triple enlace.

[20] (a) Negishi, E.; Copéret, C.; Ma, S.; Liou, S.-Y.; Liu, F. *Chem. Rev.* **1996**, *96*, 365-393. (b) Trost, B. M.; Toste, D. F.; Pinkerton, A. B. *Chem. Rev.* **2001**, *101*, 2067-2096. (c) Aubert, C.; Buisine, O.; Malacria, M. *Chem. Rev.* **2002**, *102*, 813-834. (d) Lloyd-Jones, G. C. *Org. Biomol. Chem.* **2003**, *1*, 215-236. (e) Echavarren, A. M.; Nevado, C. *Chem. Soc. Rev.* **2004**, *33*, 431-436. (f) Zhang, L.; Sun, J.; Kozmin, S. A. *Adv. Synth. Catal.* **2006**, *348*, 2271-2296. (g) Michelet, V.; Toullec, P. Y.; Genêt, J.-P. *Angew. Chem. Int. Ed.* **2008**, *47*, 2-50.

[21] (a) Schmidt, B. *Angew. Chem., Int. Ed.* **2003**, *42*, 4996-4999. (b) Diver, S. T.; Giessert, A. J. *Chem. Rev.* **2004**, *104*, 1317-1382.



Las transposiciones de esqueleto, a su vez, pueden clasificarse en dos tipos:

(a) Reacciones de metátesis, catalizadas por complejos carbénicos.

(b) Reacciones de transposición de esqueleto, catalizadas por complejos no carbénicos de metales de transición.

Sin duda, en los últimos años, las reacciones tipo tándem en las cuales un proceso de ciclación catalizado por un metal de transición y una funcionalización del ciclo formado tiene lugar en una única etapa de reacción, se ha convertido en una estrategia sintética muy importante debido a su aplicación a la síntesis de moléculas complejas empleando transformaciones altamente átomo-económicas. Cabe destacar la extensa participación del Pd como catalizador en una gran variedad de reacciones tipo tándem de ciclación-funcionalización.[22] Así, por ejemplo, las ciclaciones reductoras[23] u oxidativas[24] o las adiciones nucleófilas como las hydroxiciclaciones[25] y alcoxiciclaciones[26] han sido bien estudiadas.

Más recientemente, las reacciones de metalación[27] en las cuales tiene lugar la formación de un enlace C–C y un enlace C–M (siendo M = Si, Sn) permiten la adicional funcionalización de la molécula a través de la reactividad de dicho metal incorporado al ciclo formado.

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[22] Michelet, V.; Toullec, P. Y.; Genêt, J.-P. *Angew. Chem. Int. Ed.* **2008**, *47*, 2-50.

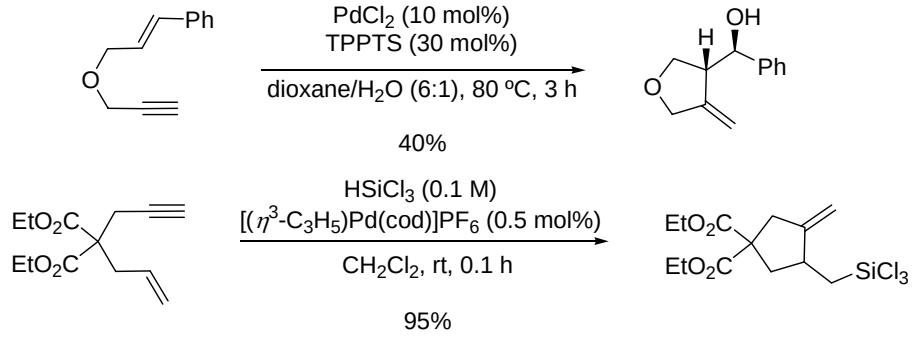
[23] (a) Trost, B. M.; Rise, F. *J. Am. Chem. Soc.* **1987**, *109*, 3161-3163. (b) Jang, H.-Y.; Krische, M. *J. Am. Chem. Soc.* **2004**, *126*, 7875-7880.

[24] (a) Tong, X.; Beller, M.; Tse, M. K. *J. Am. Chem. Soc.* **2007**, *129*, 4906-4907. (b) Weibes, L. L.; Lyons, T. W.; Cychosz, K. A.; Sanford, M. S. *J. Am. Chem. Soc.* **2007**, *129*, 5836-5837.

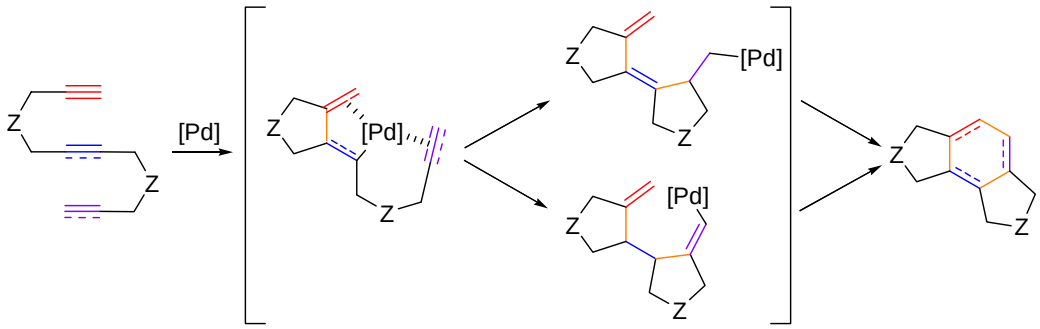
[25] Nevado, C.; Charrualult, L.; Michelet, V.; Nieto-Oberhuber, C.; Muñoz. M. P.; Méndez, M.; Rager, M.-N.; Genêt, J.-P.; Echavarren, A. M. *Eur. J. Org. Chem.* **2003**, 706-713.

[26] (a) Méndez, M.; Muñoz, M. P.; Echavarren, A. M. *J. Am. Chem. Soc.* **2000**, *122*, 11549-11550. (b) Muñoz, M. P.; Méndez, M.; Nevado, C.; Cárdenas, D. J.; Echavarren, A. M. *Synthesis* **2003**, 2898-2902.

[27] Beletskaya, I.; Moberg, C. *Chem. Rev.* **2006**, *106*, 2320-2354.



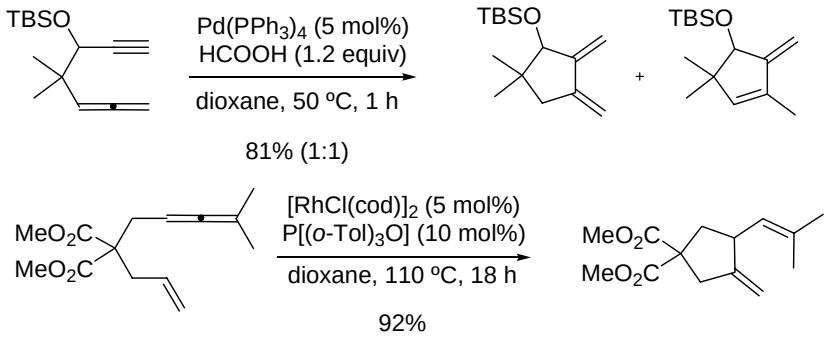
Por otra parte, la aplicación de estas estrategias de ciclación a sustratos más complejos que poseen más de dos instauraciones, permiten atrapar los complejos de metales de transición intermedios de manera intramolecular con otros dobles o triples enlaces.[28] De esta manera se obtienen compuestos policíciclicos a los cuales también se pueden aplicar las estrategias de metalación[29] y posterior funcionalización.



Por último, comparado con alquenos y alquinos, los alenos han sido mucho menos estudiados como componentes en la formación de nuevos enlaces C–C. Sin embargo, han demostrado ser intermedios muy versátiles en los últimos años.[30] Cuando una unidad de aleno se combina con un alquino o con un alqueno, se obtienen aleninos[31] y

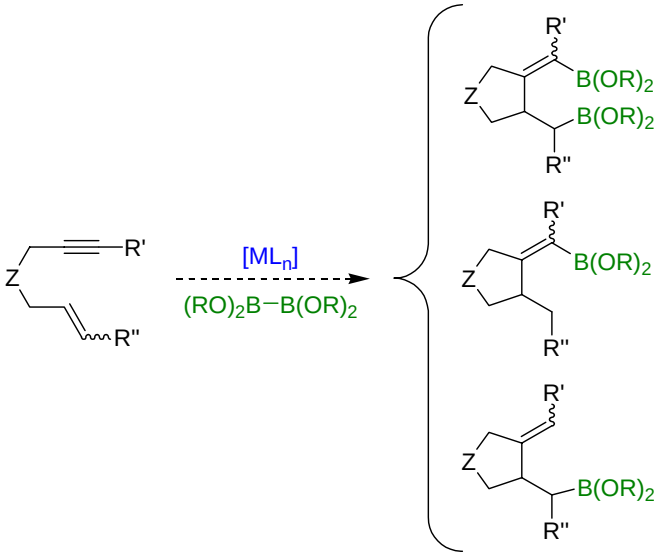
[28] (a) Trost, B. M.; Lee, D. C. *J. Am. Chem. Soc.* **1988,** *110,* 7255-7258. (b) Trost, B. M.; Shi, Y. *J. Am. Chem. Soc.* **1993,** *115,* 12491-12509.
[29] Bennacer, B.; Fujiwara, M.; Lee, S-Y.; Ojima, I. *J. Am. Chem. Soc.* **2005,** *127,* 17756-17767.
[30] (a) Hashmi, A. S. K. *Angew. Chem., Int. Ed.* **2000**, *39*, 3590-3593. (b) *Modern Allene Chemistry*; Krause, N.; Hashmi, A. S. K., Eds.; Wiley-VCH: Weinheim, Germany 2004; Vols. 1-2.
[31] Cicloisomerización de aleninos: Ti: (a) Urabe, H.; Takeda, T.; Hideura, D.; Sato, F. *J. Am. Chem. Soc.* **1997**, *119*, 11295-11305. Ru: (b) Saito, N.; Tanaka, Y.; Sato, Y. *Organometallics* **2009**, *28*, 669-671. Rh: (c) Brummond, K. M.; Chen, H.; Sill, P.; You, L. *J. Am. Chem. Soc*. **2002**, *124*, 15186-15187. Pd: (d) Oh, C. H.; Jung, S. H.; Park, D. I.; Choi, J. H. *Tetrahedron Lett*. **2004**, *45*, 2499-2502. Pt: (e) Zriba, R.; Gandon, V.; Aubert, C.; Fensterbank, L.; Malacria, M. *Chem. Eur. J.* **2008**, *14*, 1482-1491. Au: (f) Cheong, P. H.-Y.; Morganelli, P.; Luzung, M. R.; Houk, K. N.; Toste, F. D. *J. Am. Chem. Soc*. **2008**, *130*, 4517-4526.

enalenos,[32] respectivamente. Ambos sustratos han sido estudiados en reacciones de cicloisomerización en procesos catalizados por metales de transición y presentan diferentes caminos de reacción dependiendo del metal empleado, y sobretodo, por la diferente reactividad que existe entre alquinos, alenos y alquenos.



Además, procesos tipo tándem de ciclación-funcionalización han sido descritos con estos compuestos, si bien los procesos de metalación[33] han sido poco estudiados.

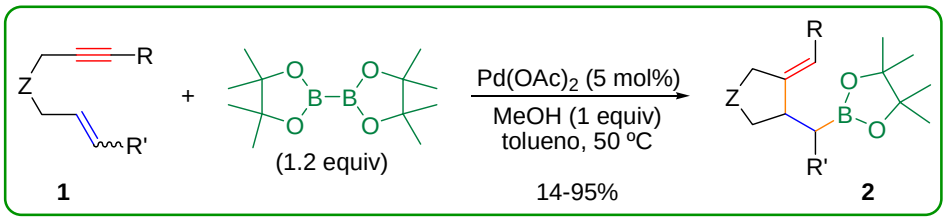
Teniendo en cuenta estos antecedentes y la necesidad de preparar nuevos compuestos de boro más elaborados con capacidad para ser aplicados en la síntesis de sustancias más complejas, el objetivo principal de esta Tesis Doctoral fue el desarrollo de una nueva reacción de ciclación borilativa de compuestos poliinsaturados.



[32] Cicloisomerización de enalenos: Ru: (a) Mukai, C.; Itoh, R. *Tetrahedron Lett.* **2006**, *47*, 3971-3974. Rh: (b) Makino, T.; Itoh, K. *J. Org. Chem.* **2004**, *69*, 395-405. Pd: (c) Närhi, K.; Franzén, J.; Bäckvall J.-E. *Chem. Eur. J.* **2005**, *11*, 6937-6943. Au: (d) Horino, Y.; Yamamoto, T.; Ueda, K.; Kuroda, S.; Toste, F. D. *J. Am. Chem. Soc.* **2009**, *131*, 2809-2811.

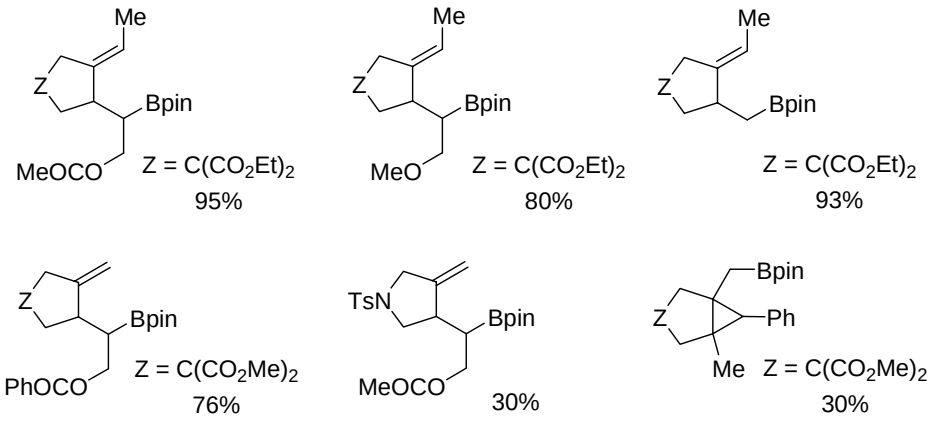
[33] Hidrosililación de aleninos: (a) Shibata, T.; Kadowaki, S.; Takagi, K. *Organometallics* **2004**, *23*, 4116-4120. Diestannilación y silisestannilación de aleninos: (b) Kumareswaran R.; Shin, S.; Gallou, I.; RajanBabu, T. V. *J. Org. Chem.* **2004**, *69*, 7157-7170.

El objetivo principal del trabajo se abordó llevando a cabo la reacción con 1,6-eninos en presencia de bis(pinacolato)diboro y con diferentes catalizadores de Pd. Los estudios preeliminares dieron lugar a una 1,7-hidroboración formal del enino de partida conduciendo a la obtención de alquilboronatos homoalílicos con rendimientos bajos (ca. 20%) junto con otros productos derivados de procesos de *β*-eliminación. La optimización de la reacción puso de manifiesto que las mejores condiciones eran aquellas que empleaban $Pd(OAc)_2$ (5 mol%) como precatalizador, bis(pinacolato)diboro (B_2pin_2, 1.2 equiv) y MeOH (1 equiv) en tolueno a 50 ºC.[34]



En el proceso tiene lugar la formación de un nuevo enlace C–C y otro C–B, y la formación de dos nuevos centros asimétricos de manera estereoespecífica.

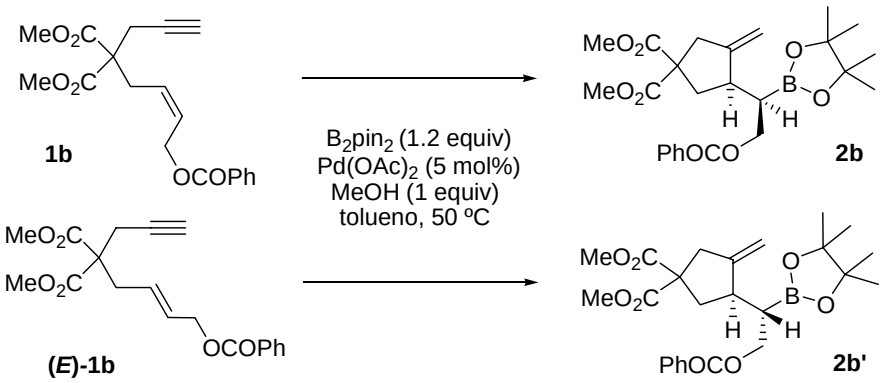
El proceso resultó ser general, y dio lugar a una gran variedad de alquilboronatos a partir de diferentes tipos de eninos. Así, tanto eninos terminales como internos con diferente sustitución en el triple enlace, dobles enlaces con grupos coordinantes en posición alílica (éteres y acetatos) y grupos no coordinantes dieron la reacción con rendimientos de moderados a muy buenos. También se ensayaron eninos con diferentes puentes en la cadena carbonada (malonato, éter, amida, bis(sulfonil)metano, metileno), obteniéndose los mejores resultados para los malonatos.



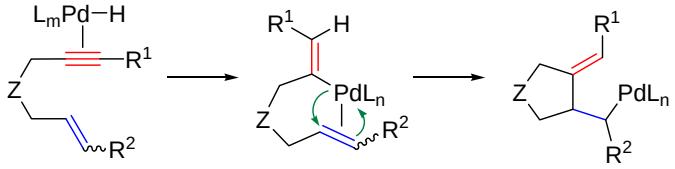
[34] Marco-Martínez, J.; López-Carrillo, V.; Buñuel, E.; Simancas, R.; Cárdenas, D. J. *J. Am. Chem. Soc.* **2007**, *129*, 1874-1875.

Además, hay que destacar que se obtuvieron, aunque en cantidades moderadas, alquilboronatos derivados de ciclopropano (ca. 30%).

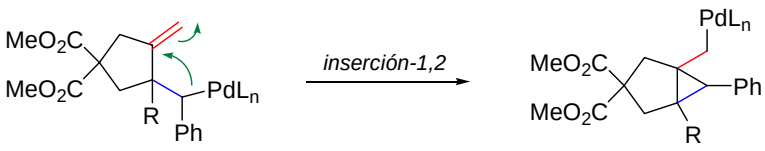
La estereoespecificidad de los nuevos centros formados pudo ser demostrada al llevar a cabo la reacción con el isómero *E* de los eninos **1a** y **1b**, que dieron lugar a los correspondientes diastereoisómeros. La configuración relativa de los nuevos centros fue asignada mediante la difracción de rayos X de cristales obtenidos a partir del alquilboronato **2b**.



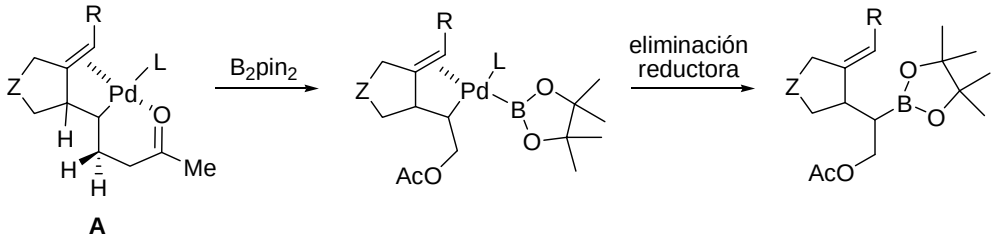
En función de los productos obtenidos, tres posibles mecanismos de reacción fueron propuestos: (a) vía inserción del triple enlace en un hidruro de Pd formado en el medio de reacción tras reducción del precatalizador de Pd(II) a Pd(0), (b) vía ciclometalación oxidante y (c) vía formación de derivados de ciclopropilcarbeno. Con el fin de obtener evidencias que apoyaran a alguna de estas posibilidades, se realizaron una serie de cálculos a nivel DFT. Los valores de energía obtenidos parecen apoyar la formación de un hidruro de Pd y posterior inserción del alquino como mecanismo más probable.



En cuanto a la formación del ciclopropano, éste podría explicarse mediante una inserción del doble enlace exocíclico en el enlace C–Pd del alquilpaladio.



Hay que destacar que la transmetalación de B_2pin_2 es más rápida que una posible *β*-eliminación en el intermedio de alquilpaladio formado (**A**) tras la ciclación. Este hecho puede deberse a la coordinación intramolecular del paladio con el doble enlace exocíclico formado y en aquellos casos en los que exista un grupo coordinante en posición alílica al doble enlace inicial, una coordinación adicional a dicho grupo.



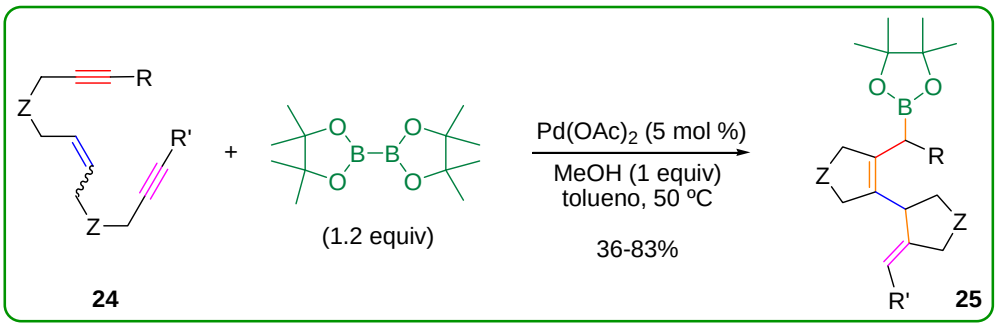
A

También hay que mencionar, que el doble enlace exocíclico resultante siempre tiene geometría *E*, debido a que la inserción del alquino en el hidruro de Pd tiene lugar de manera *syn*.

Más tarde se planteó la extensión de la reacción a sustratos en los cuales el intermedio de alquilpaladio **A** pudiera ser atrapado por otra instauración, y de esta manera llevar a cabo dos ciclaciones consecutivas con la correspondiente incorporación del Bpin.

Para ello, se llevó a cabo la reacción con 6-en-1,11-diinos en los que el resultado esperado era que tras la primera ciclación, el intermedio de alquilpaladio ciclara directamente sobre la segunda unidad de alquino y así obtener un alquenilboronato que diera lugar a alquenilboronatos.

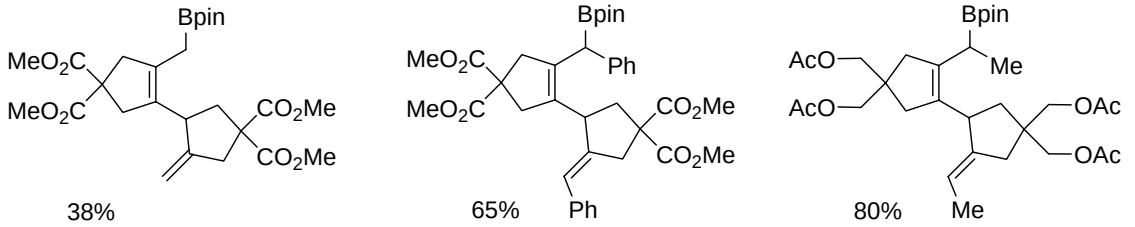
Sin embargo, cuando la reacción se llevó a cabo con estos sustratos en las condiciones optimizadas se obtuvieron alilboronatos bicíclicos, mediante la formación consecutiva de dos nuevos enlaces C–C y otro C–B.[35]



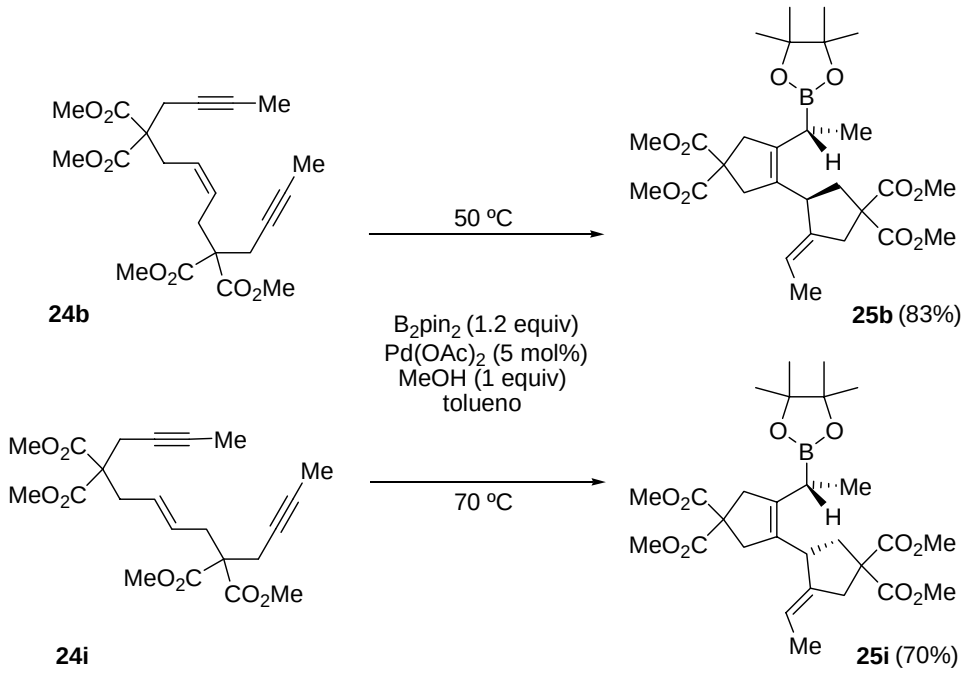
24 **25**

[35] (a) Marco-Martínez, J.; Buñuel, E.; Muñoz-Rodríguez, R.; Cárdenas, D. J. *Org. Lett.* **2008**, *10*, 3619-3621. (b) Marco-Martínez, J.; Buñuel, E.; Muñoz-Rodríguez, R.; Cárdenas, D. J. *Synfacts* **2008**, *10*, 1072-1072.

La reacción se llevó a cabo sobre diferentes tipos de 6-en-1,11-diinos, principalmente por modificación en la sustitución sobre los triples enlaces. Así, se prepararon endiinos simétricos, terminales e internos, y tanto con geometría *Z* como *E* en el doble enlace. El proceso tuvo lugar con mejores rendimientos para los alilboronatos que provenían de endiinos con geometría *Z* en el doble enlace. Sin embargo, la reacción sólo resultó satisfactoria en presencia de puentes malonato y acetato.

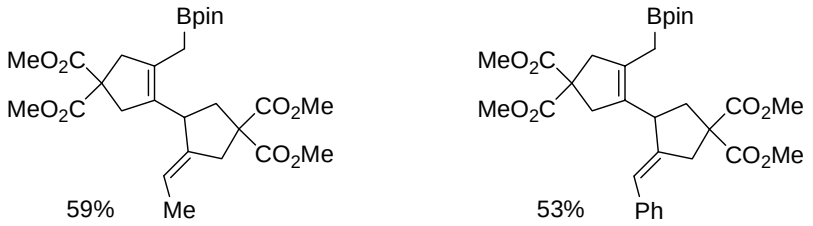


La formación de dos nuevos centros asimétricos de manera estereoespecífica pudo confirmarse al obtener productos diastereoisómeros en las reacciones de los endiinos **24b** y **24i**, por tanto la información estereoquímica de la configuración del doble enlace inicial del endiino viaja a través de los intermedios de reacción determinando la estereoquímica del producto final. La configuración relativa de los nuevos centros se determinó por difracción de rayos X de cristales obtenido a partir del alilboronato **24b**.

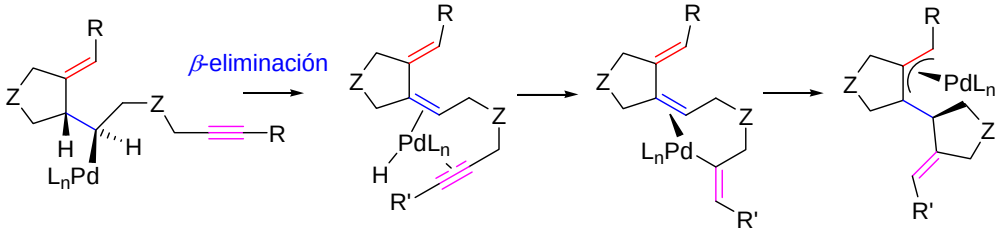


Cuando la reacción se llevó a cabo con endiinos asimétricos resultó ser regioselectiva en relación a la inserción del alquino en el hidruro de Pd, ya que los triples enlaces

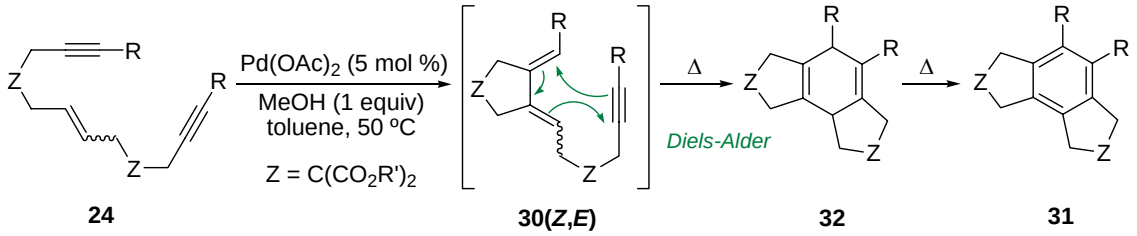
terminales eran más reactivos que los internos. Este comportamiento pudo ser también contrastado mediante cálculos a nivel DFT.



Además, la obtención de derivados 1,3-dienos cuando se llevó a cabo la reacción en ausencia de B_2pin_2 puso de manifiesto la intervención de un proceso de *β*-eliminación de hidrógeno del ciclo durante el mecanismo de reacción.

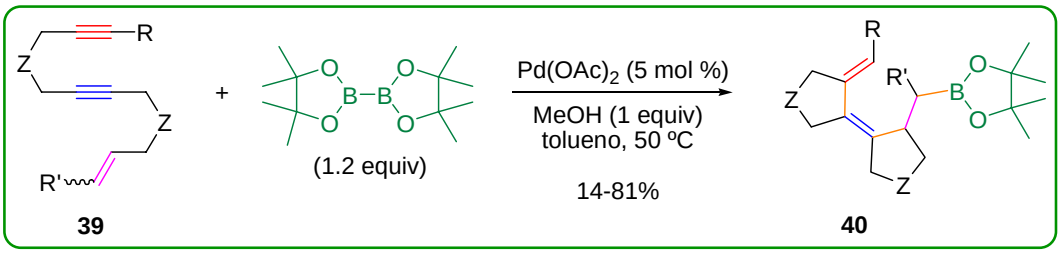


En otros casos, principalmente para los endiinos con geometría *E* en el doble enlace se obtuvieron compuestos tricíclicos, probablemente por un proceso de cicloadición de Diles-Alder intramoleclar a partir del 1,3-dieno correspondiente.

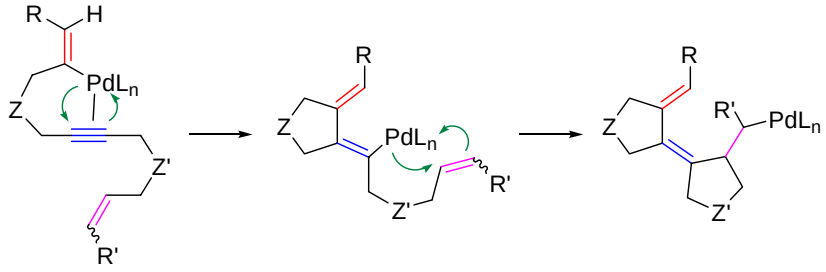


Más tarde se decidió cambiar el orden de las instauraciones, es decir, preparar 1-en-6,11-diinos, en los cuales una unidad de diino y otra de enino comparten el triple enlace que hace de puente en la molécula.

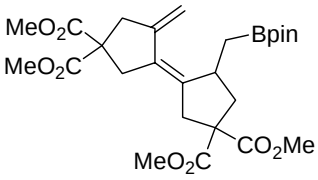
Al someter a estos nuevos endiinos a las condiciones optimizadas de reacción, se obtuvieron los esperados alquilboronatos bicíclicos por formación consecutiva de dos nuevos enlaces C–C y uno C–B.



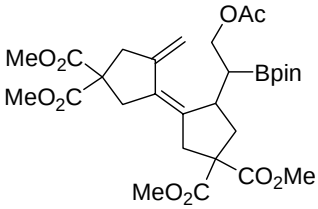
En este caso, el intermedio de alquenilpaladio formado tras la primera ciclación quedaría atrapado directamente por la unidad de doble enlace terminal, pasando a formar un intermedio de alquilpaladio, que finalmente, tras transmetalación de B_2pin_2 y eliminación reductora, darían lugar a los alquilboronatos homoalílicos obtenidos.



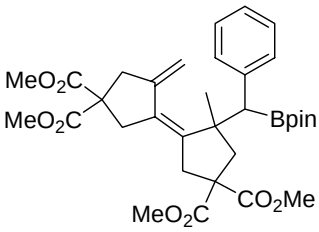
Para estudiar la generalidad de la reacción con este tipo de sustratos, se introdujeron diferentes modificaciones en el doble enlace, así se prepararon endiinos con grupos coordinantes en la posición alílica (acetatos) y no coordinantes obteniéndose rendimientos buenos cuando ambos puentes eran derivados de malonato.



60-71%

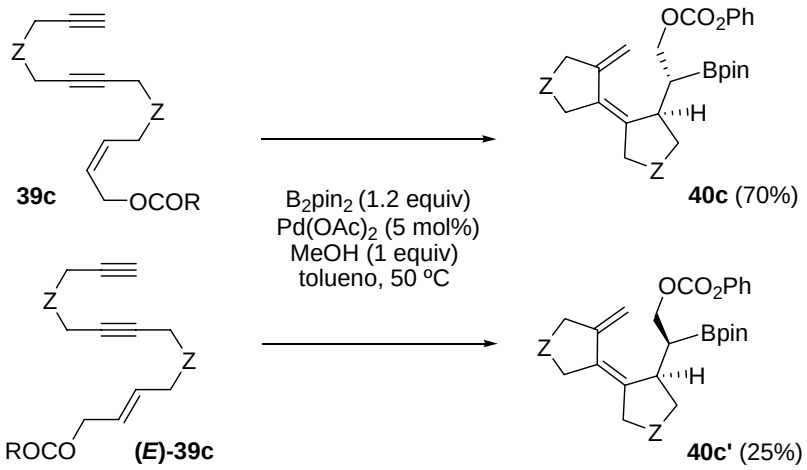


66%

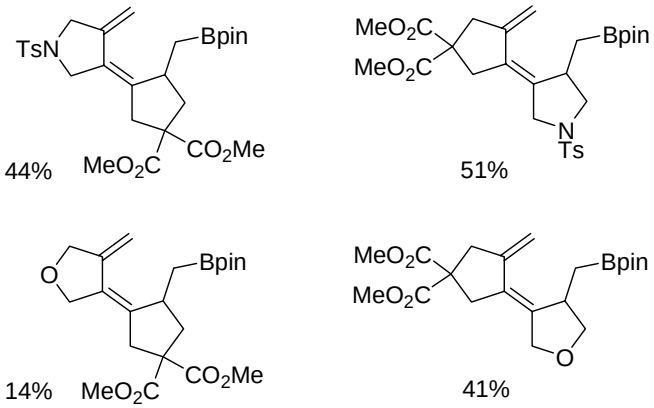


80%

La estereoespecificidad de los dos nuevos centros asimétricos formados pudo ser confirmada una vez más mediante la obtención de diastereoisómeros cuando se partía de endiinos con geometría opuesta en el doble enlace. Y la configuración relativa de los mismos se estableció a partir de la obtenida para los eninos, dado que la segunda parte del proceso es análoga.



La gran ventaja de estos sustratos fue la posibilidad de llevar a cabo la reacción con puentes diferentes a derivados de malonato, como son éter, amida, metileno o bis(sulfonil)metano. Obteniéndose mejores rendimientos cuando este tipo de puentes se encontraba situado en la unidad de enino.

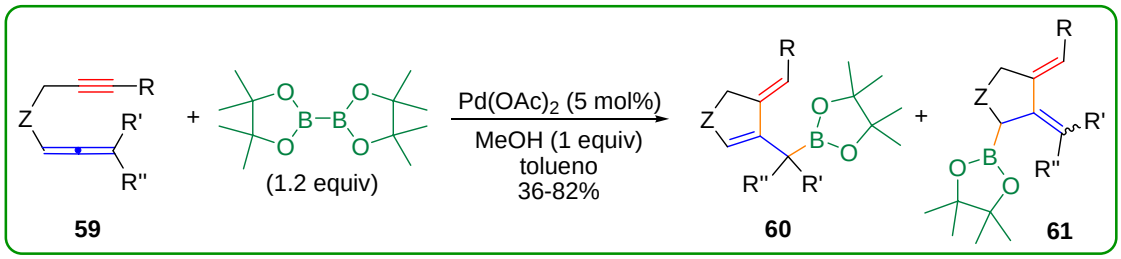


Sin embargo, cuando el alquino terminal era sustituído con diferentes grupos (Me, Ph, CO_2Me), la reacción dio lugar a mezclas de productos ya que ambas unidades de alquino interno compiten dada su similar reactividad.

Además de todos estos resultados, se decidió estudiar el comportamiento de la reacción en otra serie de sustratos más sencillos como dienos y diinos. Desafortunadamente, ninguno de los dos tipos de sustrato dio lugar a resultados satisfactorios ya que los diinos parecías sufrir procesos de polimerización dada su elevada reactividad bajo las condiciones de reacción. Por el contrario, lo dienos no reaccionaban en dichas condiciones de reacción recuperándose los sustratos de partida.

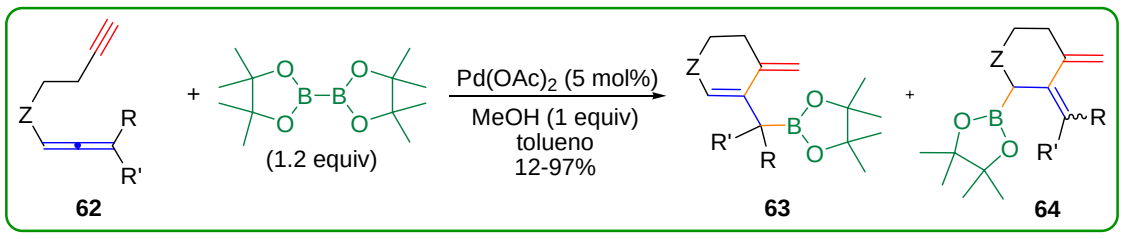
Por tanto, se llevó a cabo la preparación de 1,5- y 1,6-aleninos y 1,5-enalenos, ya que los alenos presentan una reactividad intermedia entre los alquinos y los alquenos.

Cuando los 1,5-aleninos se hicieron reaccionar en las condiciones de reacción optimizadas, se obtuvo una mezcla de dos alilboronatos, **60** y **61**, en los cuales se ha producido una ciclación para dar anillos de cinco eslabones. La formación de estos regioisómeros implica una 1,7- y una 1,5-hidroboración, respectivamente, con la correspondiente ciclación, dando lugar a un enlace C–C y un enlace C–B en una operación sencilla.[36]



En todos los casos, tanto con alquinos terminales como internos, el regioisómero mayoritario es aquel en el que el boronato se encuentra en la posición exocíclica (**60**). Hay que destacar, que se obtienen buenos rendimientos a pesar de que una posible *β*-eliminación de hidrógeno podría tener lugar en los intermedios formados durante el proceso.

Los aleninos terminales (alquino terminal) dan lugar a los correspondientes alilboronatos con rendimientos de moderados a buenos (60-82%). Mientras que los peores rendimientos fueron para los aleninos internos (alquino interno, 36-42%), posiblemente debido a la menor reactividad del alquino interno frente al aleno, y por tanto, a la potencial competitividad entre ambas insaturaciones en los primeros pasos del mecanismo de reacción.

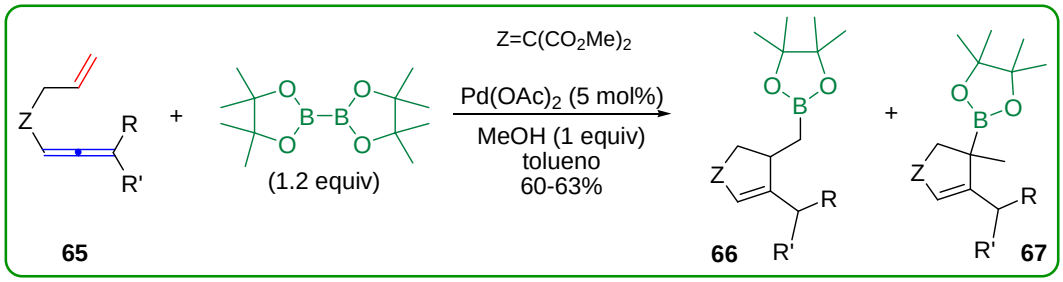


Cuando la reacción se llevó a cabo con 1,6-aleninos (**62**), homólogos a **59**, se obtuvieron los correspondientes alilboronatos de anillos de 6 eslabones, en donde se ha producido una 1,8- y una 1,6-carbociclación hidroborilativa, respectivamente. En estos

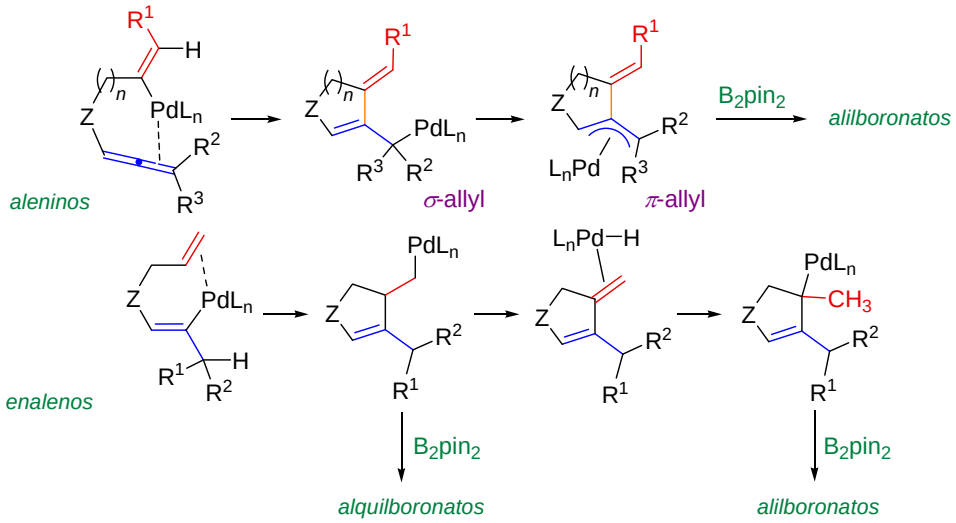
[36] Pardo-Rodríguez, V.; Marco-Martínez, J.; Buñuel, E.; Cárdenas, D. J. *Org. Lett.* **2009**, *11*, 4548-4551.

casos la regioselectividad aumentó en favor del alilboronato endocíclico llegando a ser en algunos casos el isómero mayoritario.

Análogamente, cuando la reacción se llevó a cabo sobre 1,5-enalenos (**65**), se obtuvo una mezcla de alquil- y alilboronatos (**66** y **67**) con rendimientos moderados.



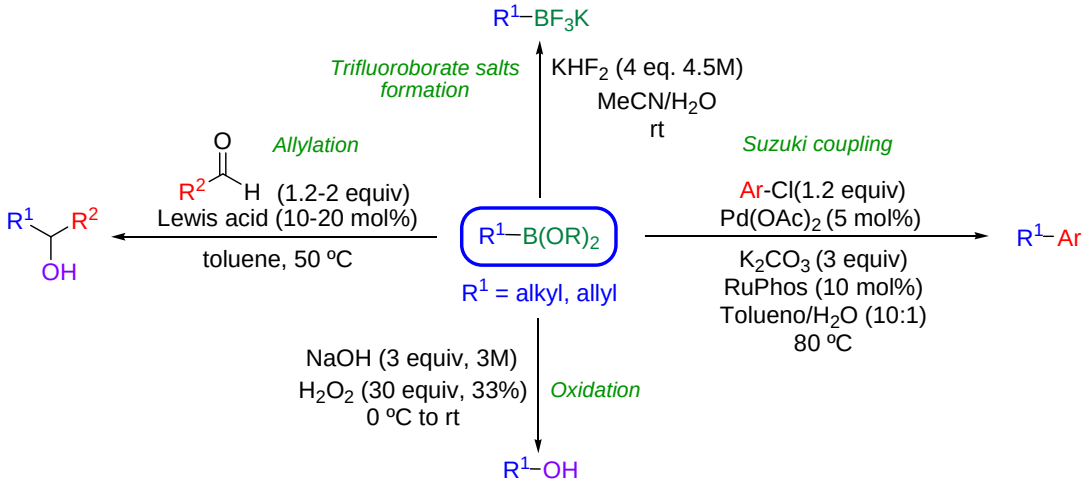
Los diferentes productos obtenidos para aleninos y enalenos muestran una diferente reactividad de las instauraciones que las constituyen, demostrando que en el caso de los aleninos la reacción comienza por el alquino, y en los enalenos la reacción comienza por el aleno. Por tanto, se puede determinar, que bajo las condiciones de reacción mencionadas, el alquino es más reactivo que el aleno, y éste último más que el alqueno.



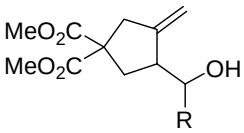
Finalmente, los alquil- y alilboronatos sintetizados a partir de cada familia de sustratos poliinsaturados, han sido también funcionalizados posteriormente. Así se han obtenido alcoholes[37] y se ha llevado a cabo la formación de nuevos enlaces C–C mediante la reacciones de alilación[38] con los alilboronatos, o reacciones de acoplamiento de

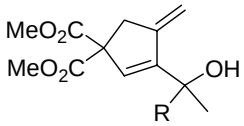
[37] Snyder, H. R.; Kuck, J. A.; Johnson, R. *J. Am. Chem. Soc.* **1938**, *60*, 105–111.
[38] (a) Rauniyar, V.; Hall, D. G. *J. Am. Chem. Soc.* **2004**, *126*, 4518–4519. (b) Carosi, L.; Lachance, H.; Hall, D. G. *Tetrahedron* **2005**, *46*, 8981-8985. (c) Hall, D. G. *Synlett* **2007**, 1644–1655.

Suzuki[39] previa preparación de las correspondientes sales de trifluoroborato[40] o ácidos borónicos.

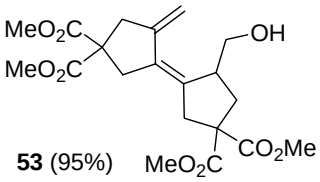


16 : R = CH_2OBz (84%)
17 : R = H (93%)

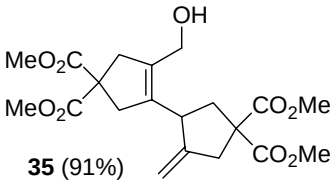




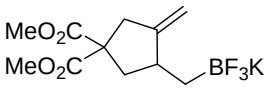
71a : R = Me (99%)
71b : R = Et (98%)



53 (95%)



35 (91%)



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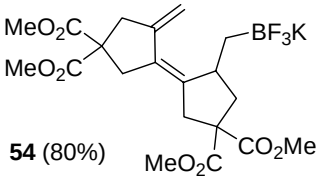
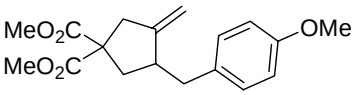
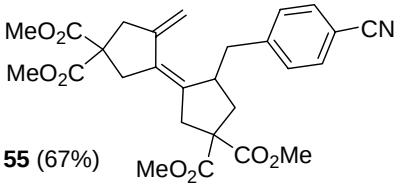


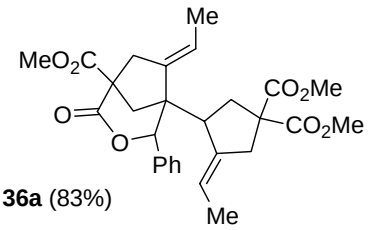
54 (80%)



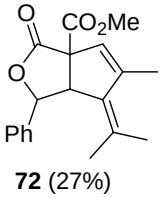
20 (50%)



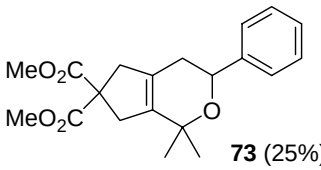
55 (67%)



36a (83%)



72 (27%)



73 (25%)

[39] Dreher, S. D.; Lim, S.-E.; Sandrock, D. L.; Molander, G. A. *J. Org. Chem.* **2009**, *74*, 3626-3631.
[40] (a) Vedejs, E.; Chapman, R. W.; Fields, S. C.; Lin, S.; Schrimpf, M. R. *J. Org. Chem.* **1995**, *60*, 3020–3027. (b) Vedejs, E.; Fields, S. C.; Hayashi, R.; Hitchcock, S. R.; Powell, D. R.; Schrimpf, M. R. *J. Am. Chem. Soc.* **1999**, *121*, 2460–2470.

A modo de conclusión, las principales aportaciones de este trabajo incluyen tanto el desarrollo de un nuevo procedimiento para la formación consecutiva de enlaces C–C y enlaces C–B, que constituyen valiosas herramientas en síntesis orgánica, como la posterior funcionalización de los boronatos cíclicos formados.

En particular pueden destacarse las siguientes aportaciones más notables:

1. Desarrollo de un procedimiento eficiente para la formación de nuevos compuestos cíclicos en los cuales el nuevo enlace C–B formado permite su posterior funcionalización, y por tanto, aumenta su potencial aplicabilidad en la síntesis de compuestos biológicamente activos.
2. Síntesis de una gran variedad de nuevos alquilboronatos y alilboronatos en condiciones suaves, evitando así el empleo de reactivos altamente básicos o nucleófilos, y compatible con un gran número de grupos funcionales.
3. Se trata de un procedimiento en cascada de ciclación-borilación que tiene lugar con baja carga de catalizador metálico y en ausencia de ligandos, dando lugar a varios enlaces en un proceso sencillo, y así altamente átomo-económico. Además de la baja toxicidad que caracteriza a los compuestos de boro.
4. La formación de nuevos centros estereogénicos de manera estereoespecífica en la reacción abre una vía para el estudio de la misma en su versión asimétrica mediante el empleo de auxiliares quirales en el medio de reacción.
5. Hay que destacar también la aportación de los estudios experimentales y computacionales que han permitido esclarecer los mecanismos por los cuales transcurre la reacción y el nuevo impulso que aportan esta serie de nuevos procesos a las ya bien estudiadas reacciones de cicloisomerización catalizada por metales de transición de compuestos poliinsaturados.

ABBREVIATIONS AND ACRONYMS

acac	acetylacetonate
Ar	aryl
Binap	2,2'-bis(diphenylphosphino)-1,1'-binaphthyl
Binol	1,1'-bi-2-naphthol
Bpin	pinacolboryl
B_2pin_2	bis(pinacolato)diboron
Bn	benzyl
br	broad
cod	cyclooctadiene
Cp	cyclopentyl
Cy	cyclohexyl
d	doublet
dba	dibenzylidenacetone
DCE	dichloroethane
DG	directing group
DIBALH	diisobutylaluminium hydride
DMAP	4-dimethylaminopyridine
DMF	*N*,*N*-dimethylformamide
DMSO	dimethyl sulfoxide
dppb	1,2-bis(diphenylphosphino)butane
dppf	1,1'- bis(diphenylphosphino)ferrocene
dtbpy	4,4'-di-tert-butyl-2,2'-bipyridyl
equiv	equivalent
ESI	electrospray
Et	ethyl
EWG	electron withdrawing group
FAB	fast-atom bombardment
GC	gas chromatography
h	hour
^{i}Pr	isopropyl
J	coupling constant (NMR)
M	molarity
m	meta
m	multiplet
Me	methyl
Mes	mesytil
mol	mole
mp	melting point
MS	mass spectroscopy
nbd	7-nitrobenzo-2-oxa-1,3-diazole
NMR	nuclear magnetic resonance
NMO	*N*-mathylmorpholine-*N*-oxide
Nu	nucleophile
o	ortho
OAc	acetate
OBz	benzoate
p	para
Ph	phenyl
Pin	pinacol
PMHS	polymethylhydroxisilane

Py	pyridine
q	quartet
Quinap	1-(2-diphenylphosphino-1-naphthyl)isoquinoline
rt	room temperature
Ruphos	2-dicyclohexylphosphino-2′,6′-diisopropoxybiphenyl
s	singlet
Segphos	5,5′-Bis(diphenylphosphino)-4,4′-bi-1,3-benzodioxole, [(4,4′-bi-1,3-benzodioxole)-5,5′-diyl]bis[diphenylphosphine]
t	triplet
^{t}Bu	*tert*-butyl
TCPC	palladacyclopentadiene tetracarboxylic acid methyl ester
$TCPC^{TFE}$	palladacyclopentadiene tetracarboxylic acid trifluoroethyl ester
$TCPC^{HBF}$	palladacyclopentadiene tetracarboxylic acid hexafluorobuthyl ester
Tol	tolyl
TPPTS	sodium triphenylphosphine trisulfonate
THF	tetrahydrofuran
Ts	4-toluenesulfonyl

INTRODUCTION

1. Boronic Acid Derivatives

From the first isolation of a boronic acid by Frankland in 1860[1] to the report of their palladium-catalyzed cross-coupling with carbon halides by Suzuki and Miyaura in 1979,[2] advances in the chemistry and biology of boronic acids have been few and far between. However, the early 1980's announced a drastic turn. In the past three decades, the status of boronic acids in chemistry has risen from peculiar and rather neglected compounds to a prime class of synthetic intermediates. Much progress has happened since the last review on boronic acid chemistry by Torssell in 1964.[3] For instance, from the discovery of rhodium-catalyzed couplings with alkenes[4] and aldehydes[5] to the commercialisation of Velcade®,[6] the first boronic acid drug used in human health therapy, new applications of boronic acids have been reported at a spectacular rate. As seen on the histogram (*Figure I*),[7] the number of publications focused on boronic acid derivatives has increased exponentially, elevating boronic acids to a new status, that of a prized class of organic compounds in chemistry and medicine.

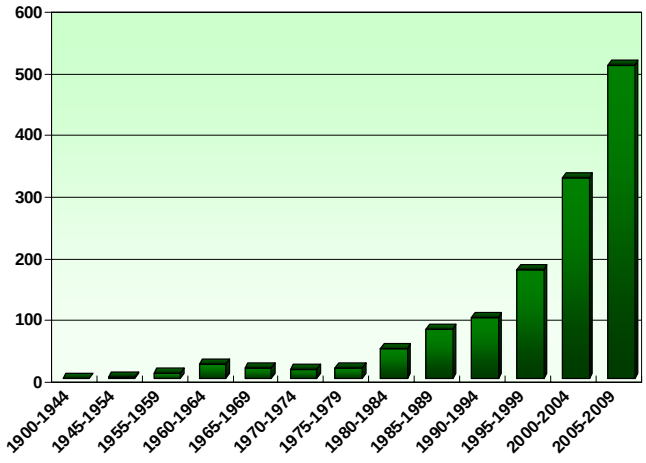


***Figure I**. Number of publications focused on boronic acids over time (Note that only those publications including the word "boronic" in their title are registered).*

[1] (a) Frankland, E.; Duppa, B. F. *Justus Liebigs Ann. Chem.* **1860**, *115*, 319-322. (b) Frankland, E.; Duppa, B. *Proc. Royal Soc. (London)* **1860**, *10*, 568-570. (c) Frankland, E. *J. Chem. Soc.* **1862**, *15*, 363-381.

[2] Miyaura, N.; Suzuki, A. *Chem. Commun.* **1979**, 866-867.

[3] Torssell, K. *Progress in Boron Chemistry*; Steinberg, H.; McCloskey, A. L., Eds.; Pergamon: New York, 1964, Volume 1, pp 369-415.

[4] Sakai, M.; Hayashi, H.; Miyaura, N. *Organometallics* **1997**, *16*, 4229-4231.

[5] Sakai, M.; Ueda, M.; Miyaura, N. *Angew. Chem., Int. Ed.* **1998**, *37*, 3279-3281.

[6] (a) Adams, J. A.; Behnke, M.; Chen, S.; Cruickshank, A. A.; Dick, L. R.; Grenier, L.; Klunder, J. M.; Ma, Y.-T.; Plamondon, L.; Stein, R. L. *Bioorg. Med. Chem. Lett*. **1998**, *8*, 333-338. (b) Paramore, A.; Frantz, S. *Nat. Rev.* **2003** (Drug Discovery), *2*, 611-612.

[7] *Boronic Acids*; Hall, D. G., Ed.; Wiley-VCH: Weinheim, Germany, 2005.

1.1 Structure and Properties

Structurally, boronic acids are trivalent boron-containing organic compounds that possess one alkyl substituent and two hydroxyl groups to fill the remaining valences on the boron atom. With only six valence electrons and a consequent deficiency of two electrons, the sp^2-hybridized boron atom possesses a vacant *p* orbital. This low-energy orbital is orthogonal to the three substituents, which are oriented in a trigonal planar geometry. Unlike carboxylic acids, their carbon analogues, boronic acids are not found in nature. These abiotic compounds are derived synthetically from primary sources of boron such as boric acid, which is made by the acidification of borax with carbon dioxide. Borate esters, the main precursors for boronic acid derivatives, are made by simple dehydration of boric acid with alcohols. Boronic acids are the products of the second oxidation of boranes. Their stability to atmospheric oxidation is considerably superior to that of borinic acids, which result from the first oxidation of boranes. The product of a third oxidation of boranes, boric acid, is a very stable and a relatively benign compound to humans (*Figure II*).

Their unique properties as mild organic Lewis acids and their mitigated reactivity profile, coupled with their stability and ease of handling, makes boronic acids a particularly attractive class of synthetic intermediates. Moreover, because of their low toxicity and their ultimate degradation into the environmentally friendly boric acid, boronic acids can be regarded as "green" compounds. They are solids that tend to exist as mixtures of oligomeric anhydrides, in particular the cyclic six-membered boroxines. For this reason and other considerations the corresponding boronic esters are often preferred as synthetic intermediates (*Figure II*).

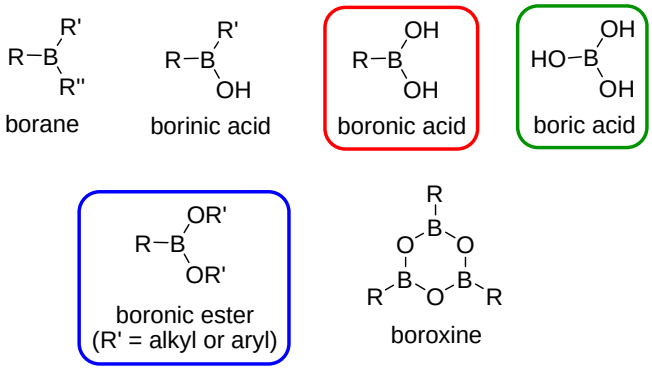


Figure II. *Oxygenated organoboron compounds.*

1.2 General Types of Boronic Acid Derivatives

The reactivity and properties of boronic acid derivatives are highly dependent upon the nature of their single variable substituent, more specifically, by the type of carbon group directly bonded to boron. By this way, boronic acids are classified in subtypes such as alkyl-, alkenyl-, alkynyl-, and aryl- boronic acids.

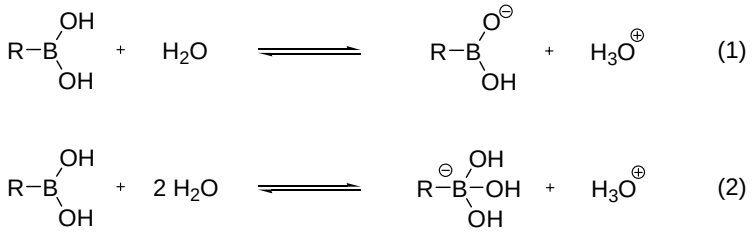
1.2.1 Boronic Acids

Most boronic acids exist as white crystalline solids that can be handled in air without special precautions. At ambient temperature, boronic acids are chemically stable and most display shelf stability for long periods. They do not tend to disproportionate into their corresponding borinic acid and boric acid even at high temperatures (thermodynamically unfavored process).[8] To minimize atmospheric oxidation and autoxidation (kinetically slow process), however, they should be stored under an inert atmosphere, although most boronic acids can be manipulated in air and are stable in water over a wide pH range. When dehydrated, either with a water-trapping agent or through co-evaporation or high vacuum, boronic acids form cyclic and linear oligomeric anhydrides such as the trimeric boroxines (*Figure II*). Fortunately, this is often inconsequential when boronic acids are employed as synthetic intermediates. Many of their most useful reactions, including the Suzuki cross-coupling, proceed regardless of the hydrated state (free boronic acid or boronic anhydride). Anhydride formation, however, may complicate analysis and characterization efforts. Furthermore, upon exposure to air, dry samples of boronic acids may be prone to decompose rapidly, and boronic anhydrides were proposed as initiators of the autoxidation process.[9] For this reason, it is often better to store boronic acids in a slightly moist state.[10] Incidentally, commercial samples tend to contain a small percentage of water that helps in their long-term preservation. Presumably, coordination of water or hydroxide ions to boron protects boronic acids from the action of oxygen.[11] Due to their facile dehydration, boronic acids tend to provide somewhat unreliable melting points. This inconvenience,

[8] Matteson, D. S. *Stereodirected Synthesis with Organoboranes*; Springer: Berlin, **1995**, pp 1-20.
[9] Snyder, H. R.; Kuck, J. A.; Johnson, J. R. *J. Am. Chem. Soc.* **1938**, *60*, 105-111.
[10] Johnson, J. R.; Van Campen, M. G., Jr.; Grummit, Jr. O. *J. Am. Chem. Soc.* **1938**, *60*, 111-115.
[11] Johnson, J. R.; Van Campen, M. G., Jr. *J. Am. Chem. Soc.* **1938**, *60*, 121-124.

and the other problems associated with anhydride formation, largely explain the popularity of boronic esters as surrogates of boronic acids.

By virtue of their deficient valence, boronic acids possess a vacant *p* orbital. This characteristic confers them unique properties as mild organic Lewis acids that can coordinate basic molecules. By doing so, the resulting tetrahedral adducts acquire a carbon-like configuration. Thus, despite the presence of two hydroxyl groups, the acidic character of most boronic acids is not that of a Brønsted acid (*Scheme I, Eq. 1*), but usually that of a Lewis acid (*Scheme I, Eq. 2*). When coordinated with an anionic ligand, although the resulting negative charge is formally drawn on the boron atom, it is in fact spread out on the three heteroatoms.



***Scheme I**. Ionization equilibrium of boronic acids in water.*

The X-ray crystal structure of phenylboronic acid was reported in 1977 by Rettig and Trotter.[12] The crystals are orthorhombic, and each asymmetric unit consists of two distinct molecules, bound through a pair of O–H---O hydrogen bonds (*Figure III*). Each dimeric ensemble is also linked with hydrogen bonds to four other similar units to give an infinite array of layers. This X-ray information also shows the different strenght between C–B (1.568 Å) and B–O (1.378 Å and 1.362 Å) bonds, being the latter shorter by the partial double bond character due to the lone pairs of oxygens and boron's vacant orbital.

The Lewis acidity of boronic acids and the hydrogen bond donating capability of their hydroxyl groups combine to lend a polar character to most of these compounds. Although the polarity of the boronic acid head can be mitigated by a relatively hydrophobic tail as the boron substituent, most small boronic acids are amphiphilic. The partial solubility of many boronic acids in both neutral water and polar organic solvents often complicates isolation and purification efforts.

[12] Rettig, S. J.; Trotter, J. *Can. J. Chem.* **1977**, *55*, 3071-3075.

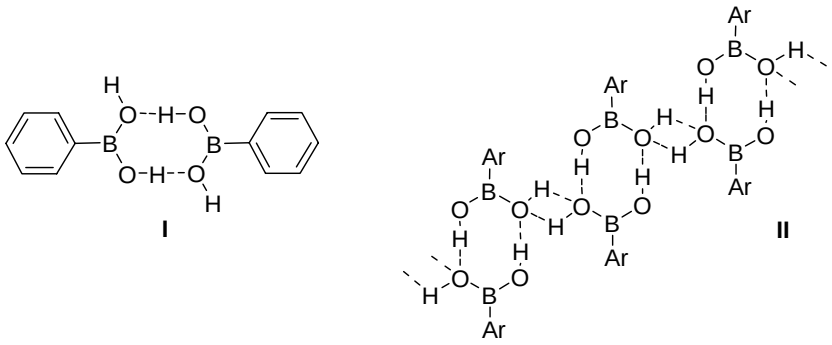


***Figure III**. Representations of the X-ray crystallographic structure of phenylboronic acid. (I) Dimeric unit showing hydrogen bonds. (II) Extended hydrogen-bonded network.*

1.2.2 Boronic Acid Derivatives

For several reasons abovementioned such as purification and characterization, boronic acids are often best handled as ester derivatives, in which the two hydroxyl groups are masked. Likewise, transformation of the hydroxyl groups into other substituents such as halides may also provide the increased reactivity necessary for several synthetic applications. Next most popular classes of boronic acid derivatives are described.

1.2.2.1 Boroxines

Boroxines are the cyclotrimeric anhydrides of boronic acids. They are isoelectronic to benzene and, by virtue of the vacant orbital on boron, may possess partial aromatic character. For instance, X-ray crystallographic analysis of triphenylboroxine confirmed that it is virtually flat.[13] Boroxines are easily produced by the simple dehydration of boronic acids, either thermally through azeotropic removal of water or by exhaustive drying over sulfuric acid or phosphorus pentoxide.[9] These compounds can be employed invariably as substrates in many of the same synthetic transformations known to affect boronic acids, but they are rarely sought as synthetic products. Samples of boroxines may also contain oligomeric acyclic analogues, and they are sensitive to autoxidation when dried exhaustively.

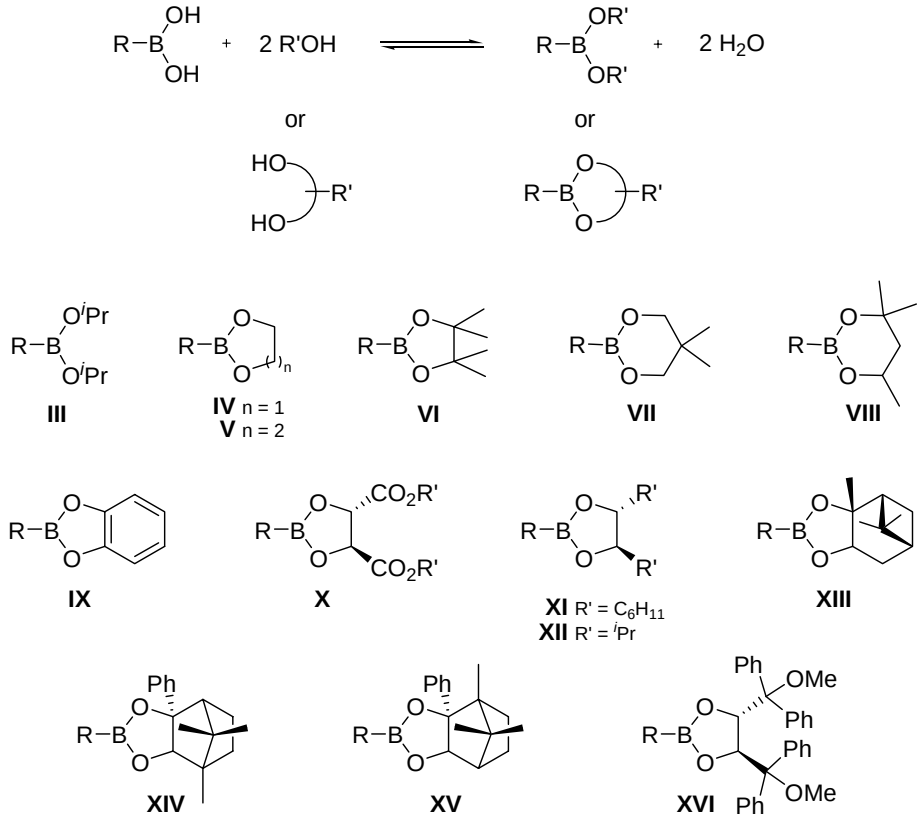
[9] Snyder, H. R.; Kuck, J. A.; Johnson, J. R. *J. Am. Chem. Soc.* **1938**, *60*, 105-111.
[13] Brock, C. P.; Minton, R. P.; Niedenzu, K. *Acta Crystallogr., Sect. C*, **1987**, *43*, 1775-1779.

1.2.2.2 Boronic Esters

By analogy with carboxylic acids, replacement of the hydroxyl groups of boronic acids by alkoxy or aryloxy groups provides esters. By losing the hydrogen bond donor capability of the hydroxyl groups, and by the partial donation of the lone pair of electrons on the oxygen atoms into the empty *p*-orbital of boron, boronic esters are less polar and easier to handle. They also serve as protecting groups to mitigate the particular reactivity of B-C bonds. Most boronic esters with a low molecular weight are liquid at room temperature and can be conveniently purified by distillation but there are crystalline solids also reported.[14] One of the most important application of boronic esters is the use of chiral derivatives as inducers in stereoselective reactions.

The synthesis of boronic esters from boronic acids and alcohols or diols is straightforward (*Scheme II*). The overall process is an equilibrium, and the forward reaction is favored when the boronate product is insoluble in the reaction solvent. Otherwise, ester formation can be driven removing the water produced (azeotropic distillation using a Dean-Stark apparatus, or using a dehydrating agent such as $MgSO_4$). Boronic esters can also be made by transesterification of smaller dialkyl esters like the diisopropyl boronates, with distillation of the volatile alcohol byproduct driving the exchange process. For cyclic esters made from the more air-sensitive alkylboronic acids, an alternate method involves treatment of a diol with lithium trialkylborohydrides.[15] Likewise, cyclic ethylboronates have been prepared by reaction of polyols with triethylborane at elevated temperatures.[16] One of the first reports on the formation of boronic esters from diols and polyols, by Kuivila and coworkers, described the preparation of several esters of phenylboronic acid by reaction of the latter, in warm water, with sugars like mannitol and sorbitol, and 1,2-diols like catechol and pinacol.[17]

[14] Ho, O. C.; Soundararajan, R.; Lu, J.; Matteson, D. S.; Wang, Z.; Chen, X.; Wei, M.; Willett, R. D. *Organometallics* **1995**, *14*, 2855-2860.
[15] Garlaschelli, L.; Mellerio, G.; Vidari, G. *Tetrahedron Lett.* **1989**, *30*, 597-600.
[16] Dahlhoff, W. V.; Köster, R. *Heterocycles* **1982**, *18*, 421-449.
[17] Kuivila, H. G.; Keough, A. H.; Soboczenski, E. J. *J. Org. Chem.* **1954**, *8*, 780-783.



***Scheme II**. Common boronic esters.*

Thermodynamically, the stability of B–O bonds in boronic acids and their ester derivatives is comparable. Consequently, hydrolysis, in bulk water or even by simple exposure to atmospheric moisture, is a threatening process while handling boronic esters that are kinetically vulnerable to attack of water. In fact, hydrolysis is very rapid for all acyclic boronic esters such as **III** (*Scheme II*), and for small unhindered cyclic ones like those made from ethylene or propylene glycol (**IV** and **V**), and tartrate derivatives (**X**).[18] Catechol esters (**IX**) are another class of popular derivatives as they are the direct products of hydroboration reactions with catecholborane. Due to the opposing conjugation between the phenolic oxygens and the benzene ring, these derivatives are more Lewis acidic and are quite sensitive to hydrolysis.

Conversely, hydrolysis can be slowed considerably for hindered cyclic aliphatic esters such as the C2-symmetrical derivatives **XI**[19] and **XII**,[20] pinacol (**VI**),[17] pinanediol

[17] Kuivila, H. G.; Keough, A. H.; Soboczenski, E. J. *J. Org. Chem.* **1954**, *8*, 780-783.
[18] (a) Haruta, R.; Ishiguro, M.; Ikeda, N.; Yamamoto, H. *J. Am. Chem. Soc.* **1982**, *104*, 7667-7669. (b) Roush, W. R.; Walts, A. G.; Hoong, L. K. *J. Am. Chem. Soc.* **1985**, *107*, 8186-8190.
[19] Ditrich, K.; Bube, T.; Stürmer, R.; Hoffmann, R. W. *Angew. Chem., Int. Ed.* **1986**, *25*, 1028-1030.
[20] Matteson, D. S.; Kandil, A. A. *Tetrahedron Lett.* **1986**, *27*, 3831-3834.

(**XIII**),[21] Hoffmann's camphor-derived diols (**XIV** and **XV**),[22] and the newer one **XVI**.[23] Indeed, many of these boronic esters tend to be stable to aqueous workups and silica gel chromatography.

1.2.2.3 Dialkoxyboranes and other Heterocyclic Boranes

Several cyclic dialkoxyboranes, such as 4,4,6-trimethyl-1,3,2-dioxaborinane **XVII**,[24] 1,3,2 benzodioxaborole (catecholborane) **XVIII**,[25] pinacolborane **XIX**,[26] have been described in the literature (*Figure IV*). Dialkoxyboranes can be synthesized simply by the reaction between equimolar amounts of borane and the corresponding diols. These borohydride reagents have been employed as hydroborating agents, in carbonyl reduction, and more recently as boronyl donors in cross-coupling reactions. Dialkoxyboranes have also been invoked as intermediates in the hydroboration of β,γ-unsaturated esters.[27] Sulfur-based heterocyclic boranes **XX**,[28] and oxazaborolidinones **XXI**[29] were also reported.

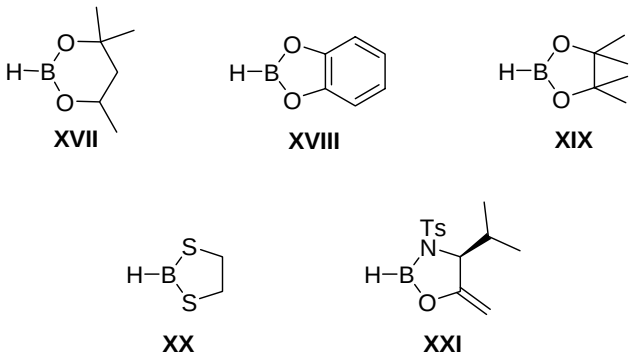
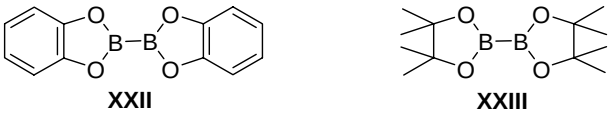


***Figure IV**. Common dialkoxyboranes and heterocyclic analogues.*

[21] Ray, R.; Matteson, D. S. *Tetrahedron Lett.* **1980**, *21*, 449-450.
[22] Herold, T.; Schrott, U.; Hoffmann, R. W. *Chem. Ber.* **1981**, *111*, 359-374.
[23] (a) Luithle, J. E. A.; Pietruszka, J. *J. Org. Chem.* **1999**, *64*, 8287-8297. (b) Luithle, J. E. A.; Pietruszka, J. *J. Org. Chem.* **2000**, *65*, 9194-9200.
[24] Woods, W. G.; Strong, P. L. *J. Am. Chem. Soc.* **1966**, *88*, 4667-4671.
[25] Brown, H. C.; Gupta, S. K. *J. Am. Chem. Soc.* **1971**, *93*, 1816-1818.
[26] Tucker, C. E.; Davidson, J.; Knochel, P. *J. Org. Chem.* **1992**, *57*, 3482-3485.
[27] Panek, J. S.; Xu, F. *J. Org. Chem.* **1992**, *57*, 5288-5290.
[28] Thaisrivongs, S.; Wuest, J. D. *J. Org. Chem.* **1977**, *42*, 3243-3246.
[29] (a) Takasu, M.; Yamamoto, H. *Synlett* **1990**, 194-196. (b) Sartor, D.; Saffrich, J.; Helmchen, G. *Synlett* **1990**, 197-198. (c) Kiyooka, S.-I.; Kaneko, Y.; Komura, M.; Matsuo, H.; Nakano, M. *J. Org. Chem.* **1991**, *56*, 2276-2278.

1.2.2.4 Diboronyl Esters

Various synthetically useful diboronyl esters have been described[30] being most commonly used such as B_2cat_2 (**XXII**) or B_2pin_2 (**XXIII**) (*Figure V*). These reagents are now commercially available, albeit their cost remains quite prohibitive for preparative applications. The discovery that diboronyl compounds can be employed with transition metal catalysts in various efficient cross-coupling and addition reactions can be considered one of the most significant advances in boronic acid chemistry in the past decade.[31]



XXII **XXIII**

Figure V. *Common diboronyl reagents.*

1.2.2.5 Dihaloboranes

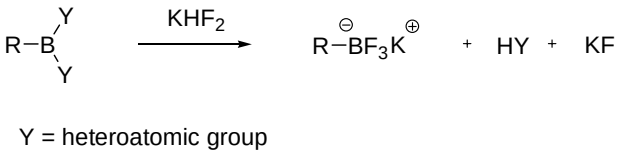
The importance of these highly electrophilic compounds relies on their capability to undergo reactions that do not affect boronic acids and esters. For example, oxidative amination of the B–C bond of boronate derivatives requires the transformation of boronic esters into the corresponding dichlorides. Of several methods described for the preparation of alkyl- and aryldichloroboranes,[32] only a few conveniently employ boronic acids and esters as substrates.

1.2.2.6 Trifluoroborate Salts

Organotrifluoroborate salts are a class of monomeric, crystalline boronic acid derivatives easily handed and indefinitely stable to moisture and air. They can be easily

[30] (a) Ishiyama, T.; Murata, M.; Ahiko, T.-A.; Miyaura, N. *Org. Synth.* **2000**, *77*, 176-182. (b) Anastasi, N. R.; Waltz, K. M; Weerakoon, W. L.; Hartwig, J. F. *Organometallics* **2003**, *22*, 365-369.
[31] (a) Marder, T. B.; Norman, N. C. *Topics Catal.* **1998**, *5*, 63-73. (b) Ishiyama, T.; Miyaura, N. *J. Organomet. Chem.* **2000**, *611*, 392-402.
[32] (a) Brown, H. C.; Salunkhe, A. M.; Singaram, B. *J. Org. Chem.* **1991**, *56*, 1170-1175. (b) Brown, H. C.; Salunkhe, A. M.; Argade, A. B. *Organometallics* **1992**, *11*, 3094-3097.

prepared according to a procedure by Vedejs and coworkers[33] and also from boronic esters[34] generating relative bening inorganic byproducts (*Scheme III*).



***Scheme III**. Synthesis of trifluoroborate salts.*

Organotrifluoroborates represent an alternative to boronic acids, boronate esters, and organoboranes for use in Suzuki-Miyaura cross-coupling[35] and other reactions such as rhodium-catalyzed 1,2- and 1,4-addition,[36] copper-promoted couplings to amines and alcohols,[37] and allylation of aldehydes.[38] Furthermore, their applications have been reviewed recently.[39] The trifluoroborate moiety is stable toward numerous reagents that are often problematic for other boron species. For instance, taking advantage of strong B–F bonds, the use of organotrifluoroborate salts may be viewed as a way to protect boron's vacant orbital from an electrophilic reaction with a strong oxidant. Consequently, remote functional groups within the organotrifluoroborates can be manipulated, while retaining the valuable C-B bond.[40]

1.3 Preparative Methods of Boronic Acids and their Esters

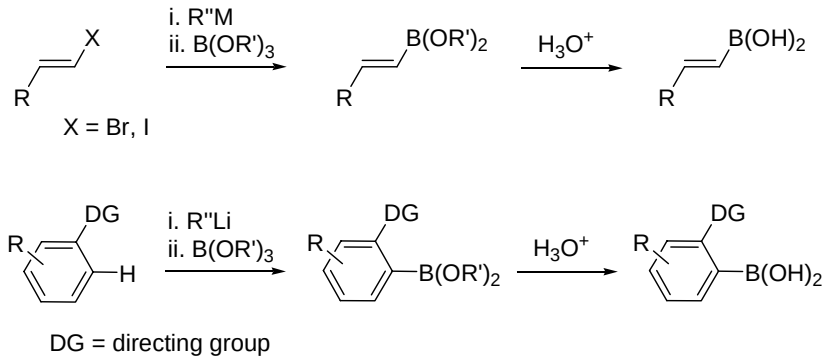
The increasing importance of boronic acids as synthetic intermediates has justified the development of new, mild and efficient methods of preparation. Several routes have been described in the literature from the historical oxidation or hydrolisis of

[33] (a) Vedejs, E.; Chapman, R. W.; Fields, S. C.; Lin, S.; Schrimpf, M. R. *J. Org. Chem.* **1995**, *60*, 3020-3027. (b) Vedejs, E.; Fields, S. C.; Hayashi, R.; Hitchcock, S. R.; Powell, D. R.; Schrimpf, M. R. *J. Am. Chem. Soc.* **1999**, *121*, 2460-2470.
[34] Matteson, D. S.; Kim, G. Y. *Org. Lett.* **2002**, *4*, 2153-2155.
[35] (a) Molander, G. A.; Ellis, N. *Acc. Chem. Res.* **2007,** *40*, 275-286. (b) Doucet, H. *Eur. J. Org. Chem.* **2008**, 2013-2030.
[36] (a) Pucheault, M.; Darses, S.; Genêt, J.-P. *Eur. J. Org. Chem.* **2002**, 3552-3557. (b) Ros, A.; Aggarwal, V. K. *Angew. Chem., Int. Ed*. **2009**, *48*, 6289-6292. (c) Gendrineau, T.; Genêt, J.-P.; Darses, S. *Org. Lett.* **2009**, *11*, 3486-3489.
[37] (a) Quach, T. D.; Batey, R. A. *Org. Lett.* **2003**, *5*, 1381-1384. (b) Quach, T. D.; Batey, R. A. *Org. Lett.* **2003**, *5*, 4397-4400.
[38] (a) Thadani, A. N.; Batey, R. A. *Org. Lett*. **2002**, *4*, 3827-3830. (b) Carosi, L.; Hall, D. G. *Angew. Chem., Int. Ed.* **2007**, *46*, 5913-5915.
[39] (a) Stefani, H. A.; Cella, R.; Vieira, A. S. *Tetrahedron* **2007**, *63*, 3623-3658. (b) Darses, S.; Genêt, J.-P. *Chem. Rev.* **2008**, *108*, 288-325.
[40] Molander, G. A.; Ribagorda, M. *J. Am. Chem. Soc.* **2003**, *125*, 11148-11149.

trialkylboranes to the direct borylation by transition metal-catalyzed C-H functionalization.

1.3.1 Trapping of Organometallic Intermediates with Borates

This method is one of the first, and probably, still the cheapest and most common way to prepare boronic acids and esters. It can be applied to the synthesis of aryl,[41] alkenyl,[42] alkynyl,[43] alkyl,[44] and allylboronic[45] acids and esters. This method involves the reaction of a hard organometallic intermediate (Li or Mg, among others) with a borate ester at low temperature (*Scheme IV*). It is just the use of this organometallic species the main drawback of the reaction due to their low functional group compability as well as the rigorously anhydrous conditions required.



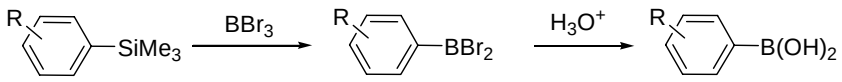
Scheme IV. *Electrophilic borate trapping of organometallic intermediate.*

In the case of arylboronic synthesis, the presence of a directing group such as amines, ethers, anilides, esters or amides leads to a direct ortho-metallation.[46]

[41] (a) Das, S.; Alexeev, V. L.; Sharma, A. C.; Geib, S. J.; Asher, S. A. *Tetrahedron Lett.* **2003**, *44*, 7719-7722. (b) Evans, D. A.; Katz, J. L.; Peterson, G. S.; Hintermann, T. *J. Am. Chem. Soc.* **2001**, *123*, 12411-12413.
[42] Brown, H. C.; Bhat, N. G. *Tetrahedron Lett.* **1988**, *29*, 21-24.
[43] Matteson, D. S.; Peacock, K. *J. Org. Chem.* **1963**, *28*, 369-371.
[44] Brown, H. C.; Cole, T. E. *Organometallics* **1983**, *2*, 1316-1319.
[45] (a) Blais, J.; L'Honoré, A.; Soulié, J.; Cadiot, P. *J. Organomet. Chem.* **1974**, *78*, 323-337. (b) Stürmer, R. *Angew. Chem., Int. Ed.* **1990**, *29*, 59-60.
[46] (a) Caron, S.; Hawkins, J. M. *J. Org. Chem.* **1998**, *63*, 2054-2055. (b) Kristensen, J.; Lysén, M.; Vedso, P.; Begtrup, M. *Org. Lett.* **2001**, *3*, 1435-1437.

1.3.2 Direct Transmetallation

Aryl[47] and alkenylboronic[48] acids can be synthetisized by direct transmetallation of trialkylsilanes and stannanes with a hard boron halide such as boron tribromide (*Scheme V*). The apparent thermodynamic drive for this reaction is the higher stability of B-C and Si (Sn)-Br bonds of products compared to the respective B-Br and Si(Sn)-C bonds of substrates.



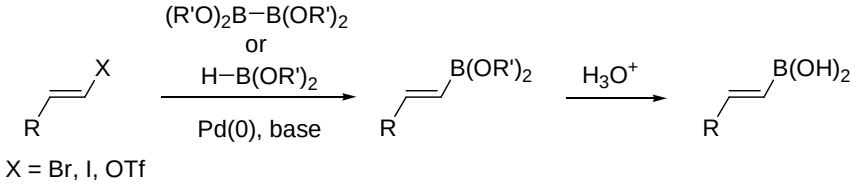
Scheme V. *Direct transmetallation*

Alkenylboronic acids can also be synthetisized from zirconocene intermediates obtained from the hydrozirconization of terminal alkynes.[49]

1.3.3 Coupling of Electrophiles and Diboronyl Reagents

This method was developed as a milder alternative to the reaction of organomagnesium or organolithium reagents. Consequently, a wider scope of substrates and functionalities could be carried out to obtain new aryl, alkenyl and allylboronic[50] acids in smooth conditions (*Scheme VI*). Miyaura and coworkers found that diboronyl esters such as B_2pin_2 (**XXIII**, *Figure V*), undergo a smooth cross-coupling reaction with bromides, iodides and triflates under palladium catalyst.[51] In the case of alkenylboronic acids, the geometry of the starting alkene is preserved in the product. Furthermore, is necessary the employ of stronger bases to achive good yields.[52]

[47] Sharp, M. J.; Cheng, W.; Snieckus, V. *Tetrahedron Lett.* **1987**, *28*, 5093-5096.
[48] Itami, K.; Kamei, T.; Yoshida, J.-I. *J. Am. Chem. Soc.* **2003**, *125*, 14670-14671.
[49] Cole, T. E.; Quintanilla, R.; Rodewald, S. *Organometallics* **1991**, *10*, 3777-3781.
[50] (a) Ishiyama, T.; Ahiko, T.-A.; Miyaura, N. *Tetrahedron Lett.* **1996**, *37*, 6889-6892. (b) Sebelius, S.; Wallner, O. A.; Sazabó, K. J. *Org. Lett.* **2003**, *5*, 3065-3068.
[51] Ishiyama, T.; Murata, M.; Miyaura, N. *J. Org. Chem.* **1995**, *60*, 7508-7510.
[52] (a) Takagi, J.; Takahashi, K.; Ishiyama, T.; Miyaura, N. *J. Am. Chem. Soc.* **2002**, *124*, 8001-8006. (b) Ishiyama, T.; Takagi, J.; Kamon, A.; Miyaura, N. *J. Organomet. Chem.* **2003**, *687*, 284-290.



***Scheme VI**. Transition metal catalyzed coupling between electrophiles and diboronyl reagents.*

The cheaper reagent pinacolborane (**XIX**, *Figure IV*), can also serve as efficient boronyl donor in this methodology.[53]

1.3.4 Hydroboration of Insaturated Compounds

Since its discovery by Brown and Rao in 1956, hydroboration chemistry has been a central reaction in the preparation of organoboron compounds.[54] There are several methods of hydroboration described in the literature, uncatalyzed and transition metal catalyzed processes.[55]

1.3.4.1 Hydroboration of Alkynes

This methodology leads to alkenylboronic acids and depending on the reaction conditions the hydroboration process could be *cis* or *trans*, both ways can be carried out under uncatalyzed (*Scheme VII*) and catalyzed (*Scheme VIII*) conditions. For instance, when a terminal alkyne is subjected to non-catalyzed thermal conditions *cis*-hydroboration is carried out in a highly regioselective reaction and adds boron at the terminal carbon.[56] Although, is necessary the use of hindered boron reagents to avoid more than one addition in the process.[57] Other uncatalyzed method is the regioselective hydroboration of bromoalkynes developed by Brown and Imai.[58] Unlike thermal conditions, in this case the global process is like an indirect *trans*-hydroboration.

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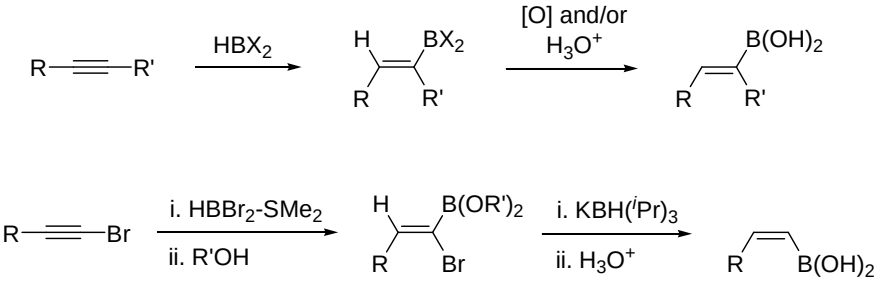
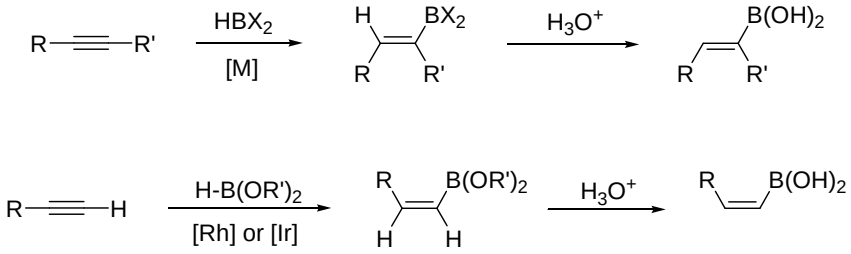
[53] (a) Murata, M.; Oyama, T.; Watanabe, S.; Masuda, Y. *J. Org. Chem.* **2000**, *65*, 164-168. (b) Murata, M.; Oyama, T.; Watanabe, S.; Masuda, Y. *Synthesis* **2000**, *6*, 778-780. (c) Murata, M.; Watanabe, S.; Masuda, Y. *Tetrahedron Lett.* **2000**, *41*, 5877-5880.
[54] (a) Brown, H. C.; Subba Rao, B. C. *J. Am. Chem. Soc.* **1956**, *78*, 5694-5695. (b) Brown, H. C. *Hydroboration*; Benjamin/Cummings: Reading MA, 1962.
[55] Beletskaya, I.; Pelter, A. *Tetrahedron Lett.* **1997**, *53*, 4957-5026.
[56] (a) Brown, H. C.; Gupta, S. K. *J. Am. Chem. Soc.* **1975**, *97*, 5249-5255. (b) Hoffmann, R. W.; Dresely, S. *Synthesis* **1988**, 103-106.
[57] Brown, H. C.; Zweifel, G. *J. Am. Chem. Soc.* **1961**, *83*, 3834-3840.
[58] Brown, H. C.; Imai, T. *Organometallics* **1984**, *3*, 1392-1395.



Scheme VII. *Uncatalyzed hydroboration of alkynes.*

On the other hand, transition metal catalyzed *cis*-hydroboration has been also reported with different catalysts (i.e. Ti, Zr, Rh, Ni)[59] using pinacolborane as hydroborating reagent. This reaction has been applied also to allenes affording alkenylboronic esters.[60] Finally, Miyaura and coworkers found the way to obtain *cis*-alkenylboronic acids by a direct *trans*-hydroboration in a Rh or Ir catalyzed reaction.[61]



Scheme VIII. *Catalyzed hydroboration of alkynes.*

1.3.4.2 Hydroboration of Alkenes

Both catalyzed and uncatalyzed hydroboration processes mentioned above serve as powerful methods to access alkylboronic esters when an alkene is employed in the reaction.[62] The asymmetric hydroborations of alkenes with chiral hydroborating reagents[63] or chiral rhodium catalyst[64] constitute well-established routes to access chiral alkylboronic esters or the corresponding alcohols or amines after a stereoespecific oxidation of the B-C bond.

[59] Ti: (a) He, X.; Hartwig, J. F. *J. Am. Chem. Soc.* **1996**, *118*, 1696-1702. Zr: (b) Pereira, S.; Srebnik, M. *Organometallics* **1995**, *14*, 3127–3128. Rh and Ni: (c) Pereira, S.; Srebnik, M. *Tetrahedron Lett.* **1996**, *37*, 3283-3286.
[60] Yamamoto, Y.; Fujikawa, R.; Yamada, Y.; Miyaura, N. *Chem. Lett.* **1999**, 1069-1070.
[61] Ohmura, T.; Yamamoto, Y.; Miyaura, N. *J. Am. Chem. Soc.* **2000**, *122*, 4990-4991.
[62] Männig, D.; Nöth, H. *Angew. Chem., Int. Ed.* **1985**, *24*, 878-879.
[63] Brown, H. C.; Singaram, B. *Acc. Chem. Res.* **1988**, *21*, 287-293.
[64] Crudden, C. M.; Hleba, Y. B.; Chen, A. C. *J. Am. Chem. Soc*. **2004**, *126*, 9200-9201.

Furthermore, when 1,3-butadienes[65] and allenes[66] are subjected under transition metal catalyzed conditions (i.e. Pd, Rh or Pt) in the presence of an hydroborating reagent the corresponding allylboronic esters are achieved.

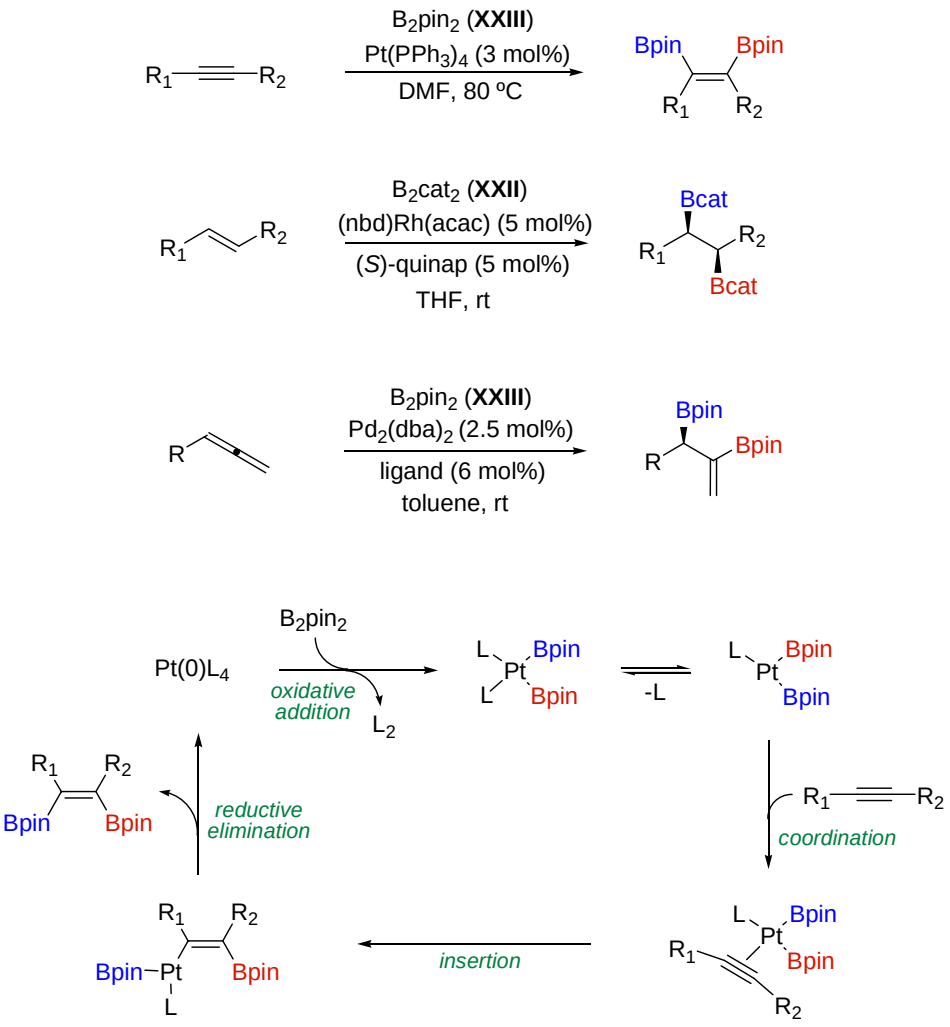
1.3.5 Bismetallatation of Insaturated Compounds

Another interesting preparation method of alkenyl, alkyl and allylboronic esters, developed in past two decades, is the transition metal catalyzed reaction (i.e. Pd, Pt, Ni, Rh) of alkynes, alkenes, dienes and allenes with bimetallic reagents of the main group elements (M-M', M = B, M' = Si, Sn, B, etc). Thereby, more elaborated boronyl-substrates, with higher synthetic versatility, are obtained with the possibility of further selective functionalization.

By this way, diboration[67] of alkynes,[68] dienes[69] and enantioselective diboration of alkenes[70] and allenes[71] have been described in the literature (*Scheme IX*). Borylsilylation[72] and borylstannylation,[73] among others, have been also reported (*Scheme X*).

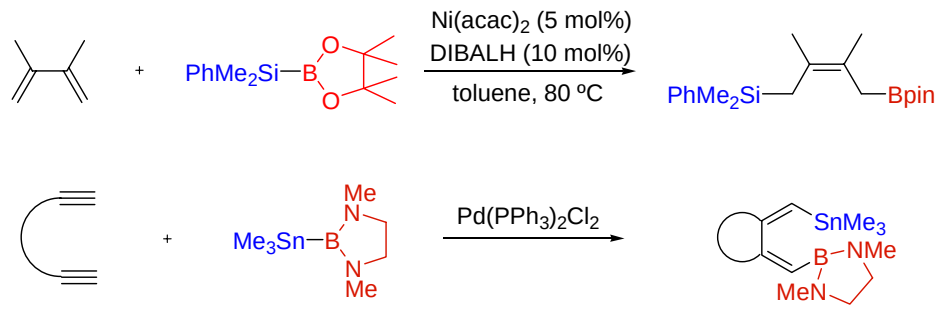
General mechanistic pathway requires an oxidative addition of the bimetallic reagent to the catalyst, followed by coordination and insertion of the insaturated C-C bond into one of the Pd–M bond and finally reductive elimination of the second B-M' bond (*Scheme IX*). Regioselectivity of the process depends on both sterical and electronic factors and can be modulated by the use of different catalyst conditions.

[65] Satoh, M.; Nomoto, Y.; Miyaura, N.; Suzuki, A. *Tetrahedron Lett.* **1989**, *30*, 3789-3792.
[66] Yamamoto, Y.; Fujikawa, R.; Yamada, A.; Miyaura, N. *Chem. Lett.* **1999**, 1069-1070.
[67] (a) Marder, T. B.; Norman, N. C. *Top. Catal.* **1998**, *5*, 63-73. (b) Ishiyama, T.; Miyaura, N. *J. Organomet. Chem.* **2000**, *611*, 392-402.
[68] Ishiyama, T.; Matsuda, N.; Murata, M.; Ozawa, F.; Suzuki, A.; Miyaura, M. *Organometallics* **1996**, *15*, 713-720.
[69] Ishiyama, T.; Yamamoto, M.; Miyaura, N. *Chem. Commun.* **1996**, 2073-2074.
[70] Morgan, J. B.; Miller, S. P.; Morken, J. P. *J. Am. Chem. Soc.* **2003**, *125*, 8702-8703.
[71] Burks, H. E.; Liu, S.; Morken, J. P. *J. Am. Chem. Soc.* **2007**, *129*, 8766-8773.
[72] Of alkynes: (a) Onozawa, S.; Hatanaka, Y.; Tanaka, M. *Chem. Commun.* **1997**, 1229-1230. Of allenes: (b) Ohmura, T.; Taniguchi, H.; Suginome, M. *J. Am. Chem. Soc.* **2006**, *128*, 13682-13683. Of dienes: (c) Suginome, M.; Nakamura, H.; Matsuda, T.; Ito, Y. *J. Am. Chem. Soc.* **1998**, *120*, 4248-4249.
[73] Of alkynes: (a) Onozawa, S.; Hatanaka, Y.; Sakakura, T.; Shimada, S.; Tanaka, M. *Organometallics* **1996**, *16*, 5450-5452. Of allenes: (b) Onozawa, S.; Hatanaka, Y.; Tanaka, M. *Chem. Commun.* **1999**, 1863-1864.



Scheme IX. *Diboration of insaturated compounds and catalytic cycle.*

This methodology is also useful with poliinsaturated compounds such as enynes[74] or diynes[75] since the bismetallation process is accompanied by a cyclization (*Scheme X*). Normally, carbocyclization takes places after the insertion of the first metal moiety.

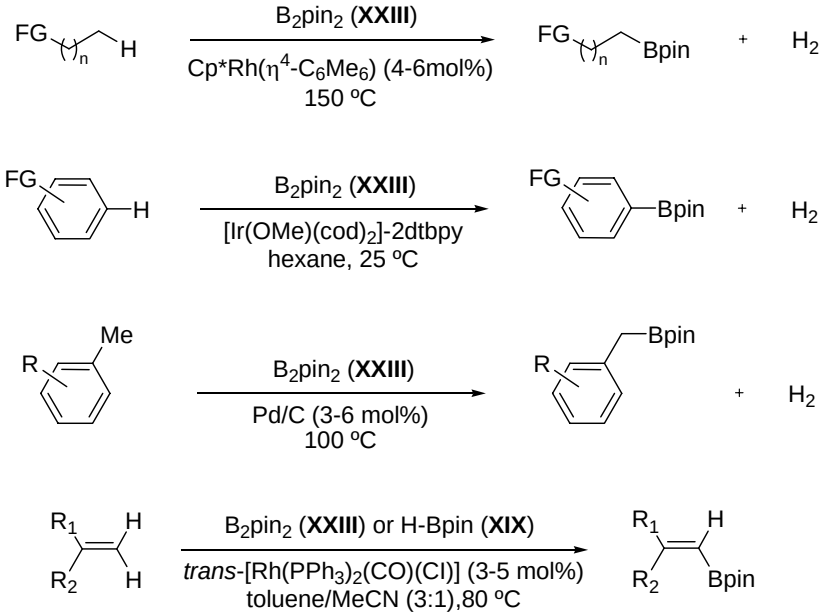


Scheme X. *Bismetallation of poliinsaturated compounds.*

[74] Mori, M. ; Hirose, T.; Wakamatsu, H.; Imakuni, M.; Sato, Y. *Organometallics* **2001**, *20*, 1907-1909.
[75] Onozawa, S.; Hatanaka, Y.; Choi, N.; Tanaka, M. *Organometallics* **1997**, *16*, 5389-5391.

1.3.6 Direct Borylation by C–H Bond Activation

Direct borylation of hydrocarbons catalyzed by a transition metal complex has been also studied and has become an economical, efficient, elegant, and environmentally benign protocol for the synthesis of a variety of organoboron compounds. Several transition metals (i.e. Re, Rh, Ir, Ru, Pd) catalyzed C–H borylation of alkanes, alkenes, arenes and benzylic positions of alkylarenes by a boron donor reagent (i.e. H-Bpin, **XIX** and B_2pin_2, **XXIII**) and provide alkyl, alkenyl, aryl or heteroaryl and benzylboron compounds, respectively (*Scheme XI*).



***Scheme XI**. Direct borylation by C–H bond activation.*

The concept of this type of direct borylation was first demostrated on alkanes by Hartwig using photochemical conditions (Re),[76] although thermal conditions (Rh and Ru)[77] have been also reported with these substrates. For arene compounds, several research groups have developed a number of efficient procedures using Re,[76b] Rh[78] and

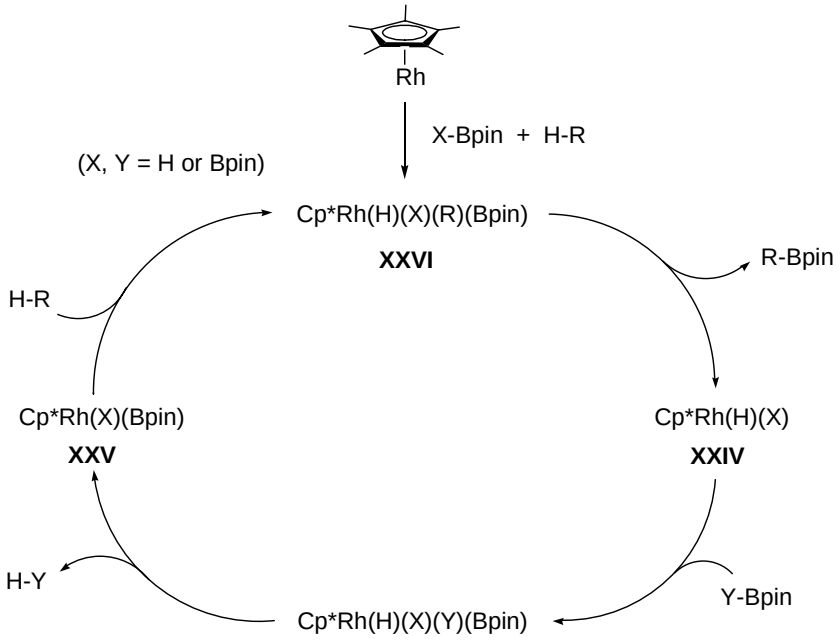
[76] (a) Waltz, K.M.; Hartwig, J. F. *Science* **1997**, *277*, 211-213. (b) Chen, H.; Hartwig, J. F. *Angew. Chem., Int. Ed.* **1999**, *38*, 3391-3393.

[77] (a) For Rh: Lawrence J. D.; Takahashi M.; Bae C.; Hartwig, J. F. *J. Am. Chem. Soc.* **2004**, *126*, 15334-15335. (b)For Ru: Murphy, J. M.; Lawrence J. D.; Kawamura, K.; Incarvito, C.; Hartwig, J. F. *J. Am. Chem. Soc.* **2006**, *128*, 13684-13685.

[78] (a) Chen, H. Y.; Schlecht, S.; Semple, T. C.; Hartwig, J. F. *Science* **2000**, *287*, 1995-1997. (b) Tse, M.K; Cho, J-Y.; Smith III, M. R. *Org. Lett.* **2001**, *3*, 2831-2833.

Ir[79] catalysts, and this methodology is currently being use for polymer functionalization.[80] And finally, vinylic[81] and benzylic[82] C–H functionalization have been also described by Marder and coworkers using Rh as catalyst. The use of Pd/C catalyst affords selective benzylic C-H borylation of alkylbenzenes.[83]

Regarding to the mechanism of the process, it is worth mentioning that there are two important bonds activations: a) hydrocarbon C-H bond activation by an oxidative addition process to the catalyst and, b) B-B or B-H bond activation, depending on the boron reagent used, by transmetallation or oxidative addition as well.



***Scheme XII**. Catalytic cycle of borylation by C–H bond activation.*

For instance, in the case of Rh(I) as catalyst the mechanism has been suggested to be a Rh(III)-Rh(V) cycle involving oxidative addition of B_2pin_2 (**XXIII**) or H-Bpin (**XIX**) to a Rh(III) complex (**XXIV**), reductive elimination of H_2 or H-Bpin to form a Rh(III) species (**XXV**), oxidative addition of an alkane to the Rh(III) complex (**XXV**), and reductive elimination of a 1-borylalkane from a Rh(V) intermediate (**XXVI**) to

[79] (a) Cho, J-Y.; Tse, M.K; Holmes, D.; Maleczka, R. E.; Smith III, M. R. *Science* **2002**, *295*, 305-308. (b) Ishiyama, T.; Nobuta, Y.; Hartwig, J. F.; Miyaura, N. *Chem. Commun.* **2003**, 2924-2925. (c) Mkhalid, I. A. I.; Coventry, D. N.; Albesa-Jove, D.; Batsanov, A. S.; Howard, J. A. K.; Perutz, R. N.; Marder, T. B. *Angew. Chem.*, *Int. Ed.* **2006**, *45*, 489-491.

[80] Jo, T. S.; Kim, S. H.; Shin, J.; Bae, C. *J. Am. Chem. Soc.* **2009**, *131*, 1656-1657.

[81] Mkhalid, I. A. I.; Coupes, R. B.; Edes, S. N.; Coventry, D. N.; Souza, F. A. S.; Thomas, R. Ll.; Hall, J. J.; Bi, S.-W.; Lin, Z.; Marder, T. B. *Dalton Trans.* **2008**, 1055-1064.

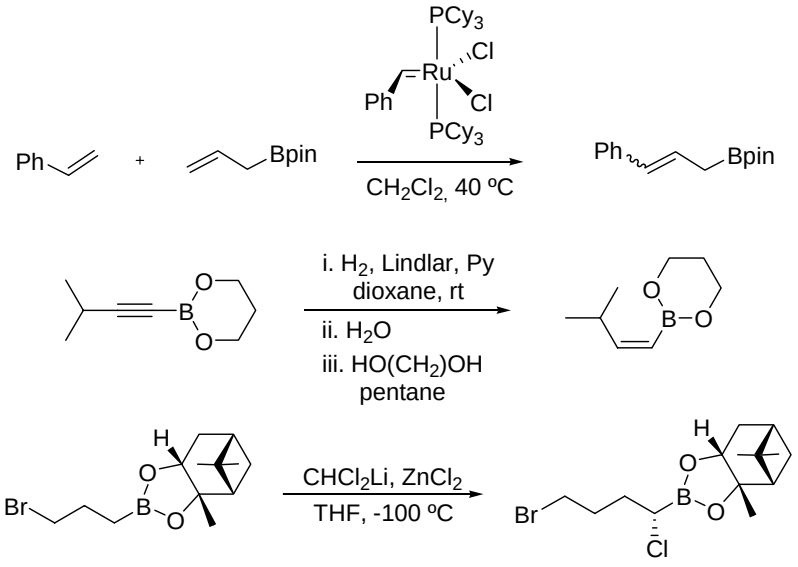
[82] Shimada, S.; Batsanov, A. S.; Howard, J. A. K.; Marder, T. B. *Angew. Chem.*, *Int. Ed.* **2001**, *40*, 2168-2171.

[83] Ishiyama, T.; Ishida, K.; Takagi, J.; Miyaura, N. *Chem. Lett.* **2001**, 1082-1083.

regenerate the Rh(III) species (**XXIV**) (*Scheme XII*).[84] These proposed processes have been supported by the results of theoretical studies.[85] For Ir, although all the mechanism is not yet well elucidated, seems to be similar to the proposed for Rh(I) and proceeds throught an Ir(III)-Ir(V) cycle according to the computational results.[86] Furthermore, several transition metal complexes have been reviewed for the use in this methodology.[87]

1.3.7 Other Methods

In addition to the methods described above, there are other valid methodologies for the synthesis of boronic acids and their esters by the modification of previous boronic derivatives. For instance, olefin metathesis[88] affords alkenylboronic and allylboronic acids and esters, hydrogenation[89] of alkynyl or alkenylboronic acids and esters leads to the corresponding allyl and alkylboronic derivatives, and finally, homologation of (α-haloalkyl)boronic esters[90] or alkenylboronates makes possible the obtaining of other alkyl and allylboronates (*Scheme XIII*).



Scheme XIII*.Other synthetic methods.*

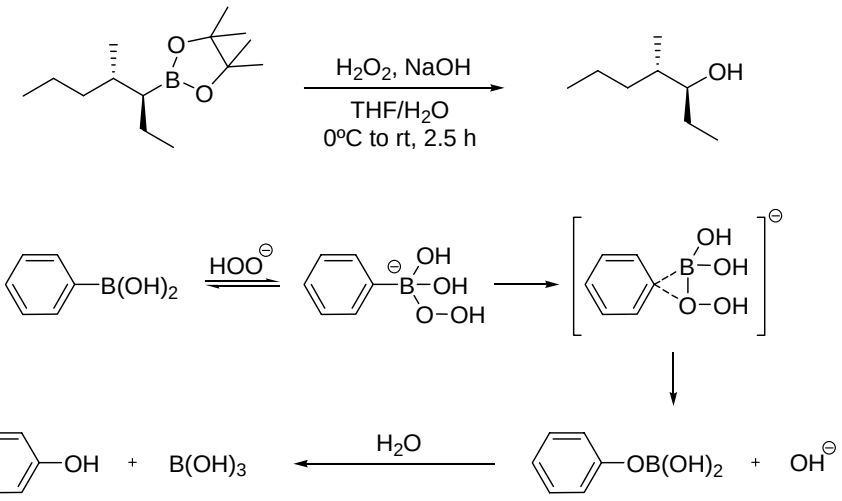
[84] Ishiyama, T.; Miyaura, N. *J. Organomet. Chem.* **2003**, *680*, 3-11.
[85] Wan, X.; Wang, X.; Luo, Y.; Takami, S.; Kubo, M.; Miyamoto, A. *Organometallics* **2002**, *21*, 3703-3708.
[86] Tamura, H.; Yamazaki, H.; Sato, H.; Sakaki, S. *J. Am. Chem. Soc*. **2003**, *125*, 16114-16126.
[87] (a) Braunschweig, H. *Angew. Chem., Int. Ed.* **1998**, *37*, 1786-1801. (b) Braunschweig, H.; Colling, M. *Coord. Chem. Rev.* **2001**, *223*, 1-51.
[88] Goldberg, S. D.; Grubbs, R. H. *Angew. Chem., Int. Ed.* **2002**, *41*, 807-810.
[89] Srebnik, M.; Bhat, N. G.; Brown, H. C. *Tetrahedron Lett.* **1988**, *29*, 2635-2638.
[90] Matteson, D. S. *Tetrahedron* **1998**, *54*, 10555-10607.

1.4 Reactions of Boronic Acid Derivatives

1.4.1 Oxidation

The treatment of boronic acids and esters with alkaline hydrogen peroxide is a classical methodology to obtain the corresponding alcohols and was developed in the first half of the past century for aryl, alkyl or alkenylboronic acid derivatives,[91] affording phenols, alkanols and aldehydes or ketones, respectively.[92] From synthetic point of view, the preparation of chiral aliphatic alcohols has a great importance since when an α-chiral alkylboronate is subjected to this oxydizing conditions proceeds with retention of configuration (*Scheme XIV*).[93]

The mechanism of the aqueous basic oxidation shows a transition state in which a boron to oxygen migration of the ipso carbon is produced (*Scheme XIV*).[94] Milder oxidants, such as anhydrous trimethylamine *N*-oxide,[95] oxone,[96] and sodium perborate[97] can also be employed of most types of boronic acid derivatives, giving the latter cleaner oxidations compared to hydrogen peroxide.

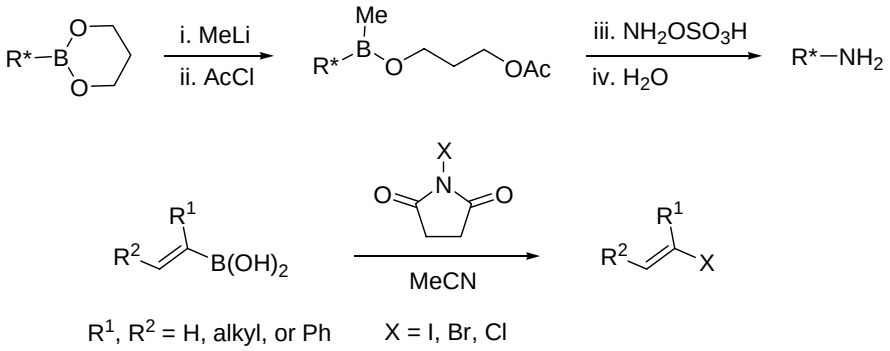


Scheme XIV. *Oxidation and mechanism.*

[91] For aryl: (a) Ainley, A. D.; Challenger, F. *J. Chem. Soc.* **1930**, 2171-2180. For alkyl and alkenyl: (b) Snyder, H. R.; Kuck, J. A.; Johnson, J. R. *J. Am. Chem. Soc.* **1938**, *60*, 105-111.
[92] Brown, H. C.; Basavaiah, D.; Kulkarni, S. U. *J. Org. Chem.* **1982**, 47, 3808-3810.
[93] Tripathy, P. B.; Matteson, D. S. *Synthesis* **1990**, 200-206.
[94] Kuivila, H. G.; Armour, A. G. *J. Am. Chem. Soc.* **1957**, *79*, 5659-5662.
[95] Kabalka, G. W.; Hedgecock, H. C., Jr. *J. Org. Chem.* **1975**, *40*, 1776-1779.
[96] Webb, K. S.; Levy, D. *Tetrahedron Lett.* **1995**, *36*, 5117-5118.
[97] Matteson, D. S.; Moody, R. J. *J. Org. Chem.* **1980**, *45*, 1091-1095.

Apart from oxygenation processes, exist other methods of oxidative replacement of boron that should be mentioned such as amination and halogenation. With regard to the amination process, does not exist a unique preparation method and many examples can be found in the literature.[98] It is worthy mentioned that the common methods and reagents for electrophilic amination, however, do not affect boronic acids and esters. Therefore, these processes require the intermediacy of more electrophilic boron substrates such as borinic acids or dicholoroboranes. Consequently, this species must be preparated previously to the amination reaction or even *in situ* (*Scheme XV*). One of the advantages of the reaction is the possibility to prepare optically pure primary and secondary amines.

As equal to amination, the halogenation reaction of boronic acids and esters has been reported many times and different mechanistic pathways undergoes depending on the nature of the substrate. Thereby, halogenation processes (generally, iodination, bromination and chlorination, *Scheme XV*) of aryl, alkenyl and alkylboronic acids and esters can be achieved.[99]



Scheme XV. *Amination and halogenation.*

1.4.2 C–C Bond Forming Processes

Carbon–carbon bond formation reactions are among the most important transformations in organic chemistry, as they constitute key steps in the building of more complex

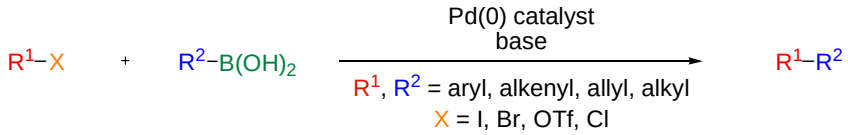
[98] (a) Brown, H. C.; Kim, K.-W.; Cole, T. E.; Singaram, B. *J. Am. Chem. Soc.* **1986**, *108*, 6761-6764. (b) Chavant, P.-Y.; Lhermitte, F.; Vaultier, M. *Synlett* **1993**, 519-521. (c) Prakash, G. K. S.; Panja, C.; Mathew, T.; Surampudi, V.; Petasis, N. A.; Olah, G. A. *Org. Lett.* **2004**, *6*, 2205-2207.

[99] For aryl: (a) Szumigala, R. H., Jr.; Devine, P. N.; Gauthier, D. R., Jr.; Volante, R. P. *J. Org. Chem.* **2004**, *69*, 566-569. For alkenyl: (b) Petasis, N. A.; Zavialov, I. A. *Tetrahedron Lett.* **1996**, *37*, 567-570. For alkyl: (c) Brown, H. C.; De Lue, R. B. *Synthesis* **1976**, 114-116.

molecules from simple precursors.[100] Organoboron compounds are involved in many C–C bond forming reactions and, this fact, makes organoboron compounds much more interesting intermediates in organic synthesis.

1.4.2.1 Pd-Catalyzed Cross-Coupling with Carbon Electrophiles (Suzuki Coupling)

The Pd-catalyzed cross-coupling reaction between organoboron compounds and organic halides or triflates provides a powerful and general methodology for the formation of C-C bonds (*Scheme XVI*). This reaction is better known as Suzuki coupling, Suzuki reaction, or Suzuki-Miyaura coupling.



***Scheme XVI**. General Suzuki-Miyaura cross-coupling.*

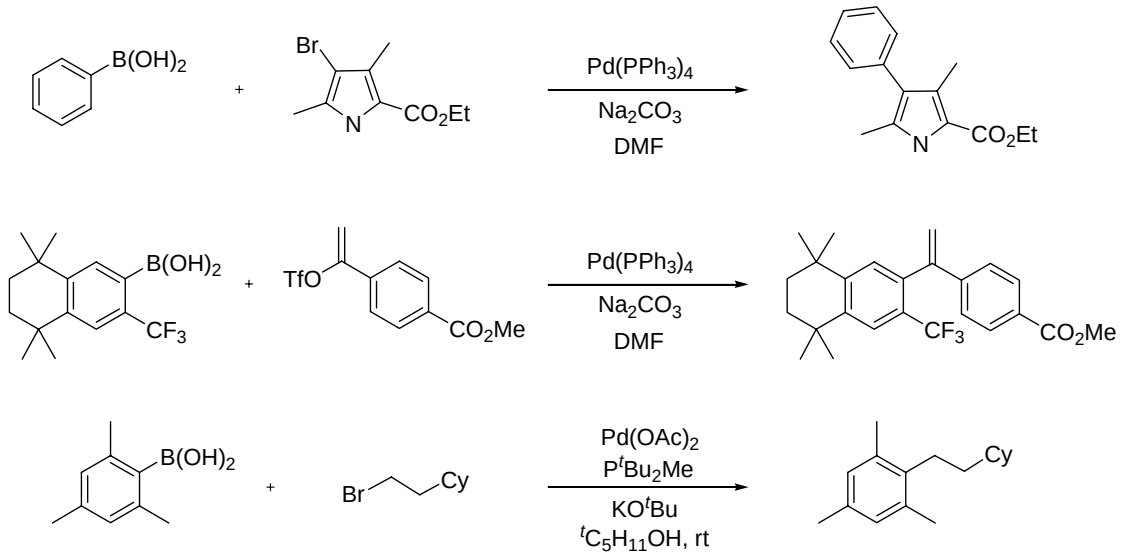
The availability of the reagents and the mild reaction conditions contribute to the versatility of this reaction. This coupling reaction offers several additional advantages, such as being largely unaffected by the presence of water, tolerating a broad range of functional groups, and proceeding generally regio- and stereoselectively. Moreover, the inorganic byproduct of the reaction is non-toxic and easily removed from the reaction mixture thereby making the Suzuki coupling suitable not only for laboratories but also for industrial processes. Undoubtedly, this reaction launched boronic acid and esters to the first line of the organic synthesis intermediates.

The reaction was first reported by Suzuki and Miyaura in 1979 describing a Pd(0)-catalyzed coupling between alkenylboranes or catecholates and aryl halides.[2] Since then, significant improvements have been made through an optimization of the different reaction parameters such as catalyst (i.e. $Pd(OAc)_2$, $Pd(PPh_3)_4$, $Pd(PPh_3)_2Cl_2$), ligands (i.e. phosphines, *N*-heterocyclic carbenes), base (i.e. Na_2CO_3, K_3PO_4, CsF), solvent (i.e. toluene, DME, THF, mixtures with H_2O), and additives (i.e. Cu_2O). Of course, these

[2] Miyaura, N.; Suzuki, A. *J. Chem. Soc., Chem. Commun.* **1979**, 866-867.
[100] *Metal-Catalyzed Cross-Coupling Reactions*; de Meijere, A.; Diederich, F., Eds.; Wiley-VCH: Weinheim, Germany, 2004.

advances have been reviewed regularly.[101] And nowadays, the reaction works with aryl, alkynyl, alkenyl and alkylboronic acids, esters and trifluoroborate salts, and a large range of electrophiles, depending on the conditions employed, being the rectivity order of the electrophilic partner established as: I >> Br > OTf >> Cl.[102]

Most commonly Suzuki coupling involve arylboronic (or heteroarylboronic) acids or esters, and aryl (or heteroaryl) electrophiles, affording symmetrical and asymmetrical biaryl compounds (*Scheme XVII*),[103] as a result of biaryl units have great importance as components of many kinds of compounds, such as pharmaceuticals, herbicides, and natural products, as well as engineering materials (i.e. conducting polymers, molecular wires, liquid crystals, etc). Moreover, arylboronic derivatives also couples with alkenyl electrophiles[104] and with non-activated alkyl halides (*Scheme XVII*).[105]



***Scheme XVII**. Arylboronic acid Suzuki couplings.*

In the case of alkynyl derivatives, compared to other organoboranes, they are stronger Lewis acids and are easily hydrolyzed. Because of these features, they have been less employed in the Suzuki coupling and need special reaction conditions, thus only

[101] (a) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457-2483. (b) Suzuki, A. *J. Organomet. Chem.* **1999**, *576*, 147-168. (c) Miyaura, N. *Top. Curr. Chem.* **2002**, *219*, 11-59. (d) Kotha, S.; Lahiri, K.; Kashinath, D. *Tetrahedron* **2002**, *58*, 9633-9695. (e) Hassan, J.; Sévignon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 1359-1469.

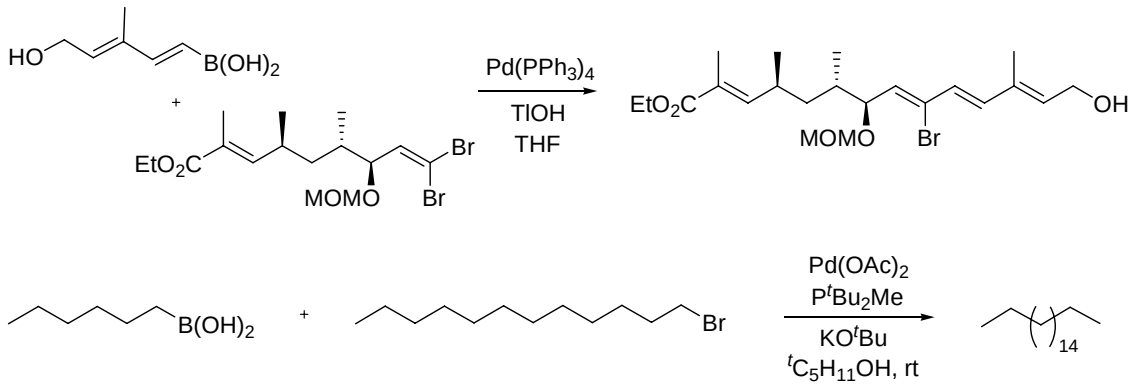
[102] Littke, A. F.; Dai, C.; Fu, G. C. *J. Am. Chem. Soc.* **2000**, *122*, 4020-4028.

[103] (a) Bencini, A.; Daul, C. A.; Dei, A.; Mariotti, F.; Lee, H.; Shultz, D.A.; Sorace, L. *Inorg. Chem.* **2001**, *40*, 1582-1590. (b) Baudoin, O. *Eur. J. Org. Chem.* **2005**, 4223-4229. (c) Yang, D. X.; Colletti, S. L.; Wu, K.; Sang, M.; Li, G. Y.; Shen, H.C. *Org. Lett.* **2009**, *11*, 381-384.

[104] Högermeier, J.; Reißig, H-U. *Chem. Eur. J.* **2007**, *13*, 2410-2420.

[105] Frisch, A. C.; Beller, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 674 -688.

alkynylboranes and alkynylborates carry out the reaction.[106] Conversely, alkenylboronic acids and esters are very useful substrates in the Suzuki coupling, in particular to access substituted olefins and dienyl moieties commonly encountered in several classes of bioactive natural products (*Scheme XVIII*).[107]



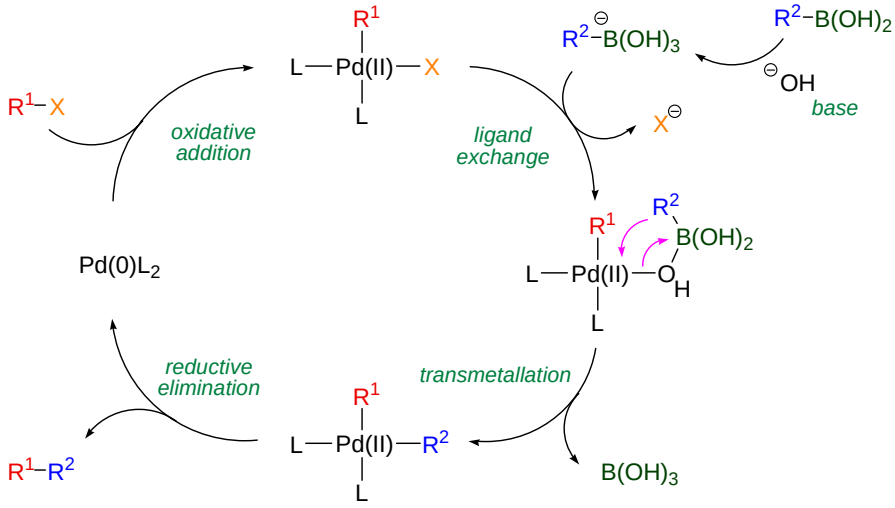
Scheme XVIII. *Alkenyl and alkylboronic acid Suzuki couplings.*

Alkylboronic acids and esters have been applied to the Suzuki coupling in the last decade as a result of the improvements on the reaction conditions since the main drawback of these substrates is their tendency to undergo *β*-hydride elimination. At present, under carefully optimized conditions even Csp^3–Csp^3 couplings between alkylboronic derivatives and alkyl electrophiles are allowed (*Scheme XIX*).[35b,108]

The accepted reaction mechanism for the aqueous basic variant involves oxidative addition of the halide substrate to give a Pd(II) intermediate, followed by a transmetallation, and a final reductive elimination that regenerates the catalyst (*Scheme XIX*).[109] The transmetallation step is thought to be facilitated by base-mediated formation of the tetracoordinate boronate anion,[110] and through a bridging hydroxyl group between the catalytic palladium center and the boron reagent. The oxidative addition step is often the rate-limiting step in a cross-coupling catalytic cycle and, in the

[35] (b) Doucet, H. *Eur. J. Org. Chem.* **2008**, 2013-2030.
[106] (a) Soderquist, J. A.; Matos, K.; Rane, A.; Ramos, J. *Tetrahedron Lett.* **1995**, *36*, 2401-2402. (b) Ishida, N.; Shimamoto, Y.; Murakami, M. *Org. Lett.* **2009**, *11*, 5434-5437.
[107] (a) Tsukamoto, H.; Sato, M.; Kondo, Y. *Chem. Commun.* **2004**, 1200-1201. (b) Peyroux, E.; Berthiol, F.; Doucet, H.; Santelli, M. *Eur. J. Org. Chem.* **2004**, 1075-1082.
[108] Chemler, S. R.; Trauner, D.; Danishefsky, S. J. *Angew. Chem., Int. Ed.* **2001**, *40*, 4544-4568.
[109] (a) Miyaura, N.; Yamada, K.; Suginome, H.; Suzuki, A. *J. Am. Chem. Soc.* **1985**, *107*, 972-980. (b) Moreno-Mañas, M.; Pérez, M.; Pleixats, R. *J. Org. Chem.* **1996**, *61*, 2346-2351.
[110] (a) Miyaura, N. *J.Organomet. Chem.* **2002**, *653*, 54-57. (b) Braga, A. C. C.; Morgon, N. H.; Ujaque, G.; Maseras, F. *J. Am. Chem. Soc.* **2005**, *127*, 9298-9307.

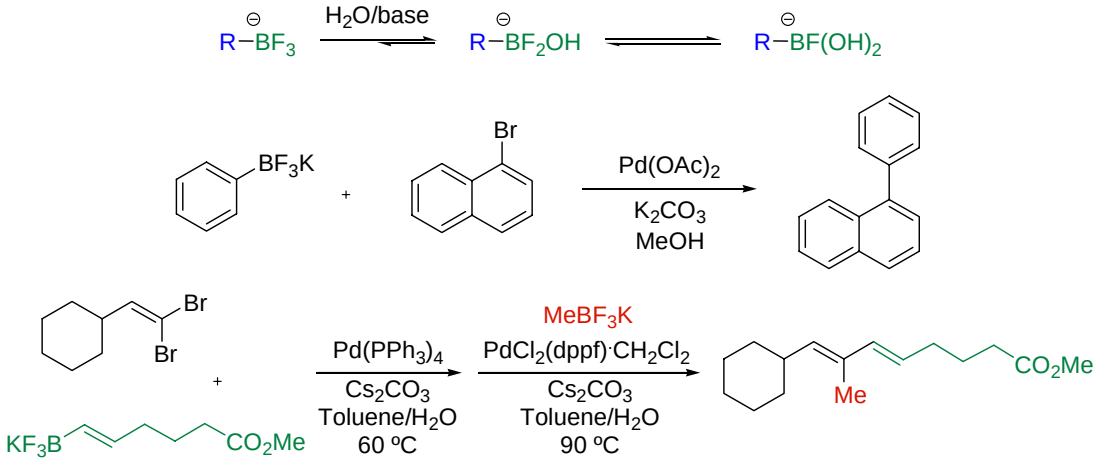
case of aryl and 1-alkenyl halides that are activated by electron-withdrawing groups this step is more reactive than those with electron-donating groups.



Scheme XIX. *Suzuki coupling catalytic cycle.*

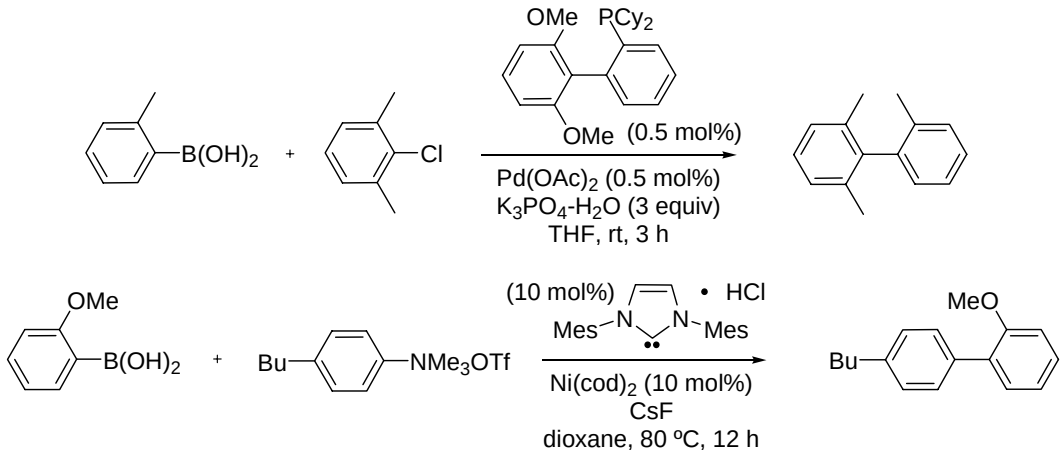
On the other hand, significant advances in the Suzuki coupling are the development and application of organotrifluoroborate salts,[35] even with primary[111] and secondary[112] alkyltrifluoroborates (*Scheme XX*). These substrates have become an important components since they allow to carry out the reaction with a wide range of electrophiles and using water as solvent or co-solvent. NMR studies[113] demostrate that fluoride/hydroxyl exchange on the organotrifluoroborate are viable, that is, one or more hidroxyl groups displace fluorides on the tetracoordinate boron species, providing intermediates that are mechanistically capable of promoting transmetalation (*Scheme XX*).

[35] (a) Molander, G. A.; Ellis, N. *Acc. Chem. Res.* **2007,** *40*, 275-286. (b) Doucet, H. *Eur. J. Org. Chem.* **2008**, 2013-2030. (c) Alacid, E.; Nájera, C. *Org. Letters*, **2008**, *10*, 5011-5014. (d) Alacid, E.; Nájera, C. *J. Org. Chem*. **2009**, *74*, 8191-8195.
[111] Dreher, S. D.; Lim, S.-E.; Sandrock, D. L.; Molander, G. A. *J. Org. Chem.* **2009**, *74*, 3626-3631.
[112] Van de Hoogenband, A.; Lange, J. H. M.; Terpstra, J. W.; Koch, M.; Visser, G. M.; Korstaje, T. J.; Jastrzebski, T. B. H. *Tetrahedron Lett.* **2008**, *49*, 4122-4124.
[113] Molander, G. A.; Biolatto, B. *J. Org. Chem.* **2003**, *68*, 4302-4314.



***Scheme XX**.Organotrifluoroborate Suzuki coupling and transmetallation species.*

Only in the past few years, several new and further improved catalyst and ligands have been developed for difficult substrates such as aryl chlorides, which are cheaper and more available than bromides.[114] Amongs other ligand advances, new phosphine based ligands[115] or phosphine free systems based on *N*-heterocyclic carbenes[116] perform very well with hindered boronic acids or electrophiles. And finally, other transition metals catalyze the reaction such as Ni or Ru, albeit the range of suitable substrates seems more limited (*Scheme XXI*).[117]

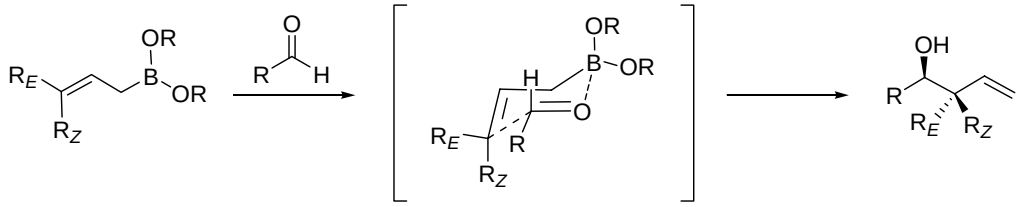


***Scheme XXI**. Other advances in the Suzuki coupling.*

[114] Littke, A. F.; Fu, G. C. *Angew. Chem., Int. Ed.* **2002**, *41*, 4176-4211.
[115] (a) Littke, A. F.; Dai, C.; Fu, G. C. *J. Am. Chem. Soc.* **2000**, *122*, 4020-4028. (b) Yin, J.; Rainka, M. P.; Zhang, X.-X.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 1162-1163. (c) Stambuli, J. P.; Kuwano, R.; Hartwig, J. F. *Angew. Chem., Int. Ed.* **2002**, *41*, 4746-4748.
[116] Navarro, O.; Kelly III, R. A.; Nolan, S. P. *J. Am. Chem. Soc.* **2003**, *125*, 16194-16195.
[117] For Ni: (a) Percec, V.; Bae, J.-Y.; Hill, D. H. *J. Org. Chem.* **1995**, *60*, 1060-1065. For Ru: (b) Na, Y.; Park, S.; Han, S. B.; Han, H.; Ko, S.; Chang, S. *J. Am. Chem. Soc.* **2004**, *126*, 250-258.

1.4.2.2 Allylation of Carbonyl Compounds

The nucleophilic addition of allylboronates to carbonyl compounds was first discovered in 1974.[118] In the case of aldehydes, the allylation produces secondary homoallylic alcohols with high stereocontrol (*Scheme XXII*). This reaction confers to these boronate reagents a special importance as a useful class of synthetic intermediates.[119]

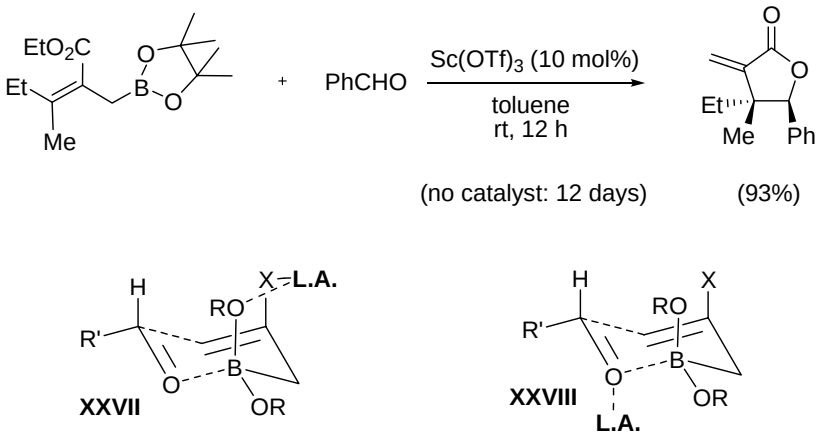


***Scheme XXII**. General reaction of allylboronates with aldehydes via a cyclic chair-like transition state.*

Allylboronates react spontaneosly with aldehydes in a non-catalyzed reaction, that is, requiring no external activator. The reaction proceeds by way of a six-membered, chair-like transition state that features a coordination bond between the boron and the carbonyl oxygen of the aldehyde (*Scheme XXII*). Brown and coworkers proposed that is the strength of this interaction the most important factor in determining the reaction rate, and the most reactive allylboronates are those with the most electrophilic boron centers.[120] Thereby, Omoto and Fujimoto performed a theoretical analysis by using an *ab initio* MO method and found a good correlation between the theoretically estimated electrophilicity of the boron center and the activation energy evaluated by the *ab initio* calculations.[121] The nucleophilicity of the γ-position of the allylboronate is also important to the reactivity of the boronate, and substituted allylboronates with groups that reduce electron density at this position are correspondingly less reactive than similar allylboronates that lack these groups. Therefore, the high stereoselectivity of the process seems to be a consequence of the compact cyclic transition state, given that this model accurately predicts the stereochemical outcome of most allylborations.

[118] Blais, J.; L'Honoré, A.; Soulié, J.; Cadiot, P. *J. Organomet. Chem.* **1974**, *78*, 323-337.
[119] (a) Denmark, S. E.; Almstead, N. G. *Modern Carbonyl Chemistry*; Otera, J., Ed.; Wiley-VCH: Weinheim, Germany, 2000; Chapter 10, p 299. (b) Chemler, S. R.; Roush, W. R. *Modern Carbonyl Chemistry*; Otera, J., Ed.; Wiley-VCH: Weinheim, Germany, 2000; Chapter 11, p 403. (c) Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207-2293.
[120] Brown, H. C.; Racherla, U. S.; Pellechia, P. J. *J. Org. Chem.* **1990**, *55*, 1868-1874.
[121] Omoto, K.; Fujimoto, H. *J. Org. Chem.* **1998**, *63*, 8331-8336.

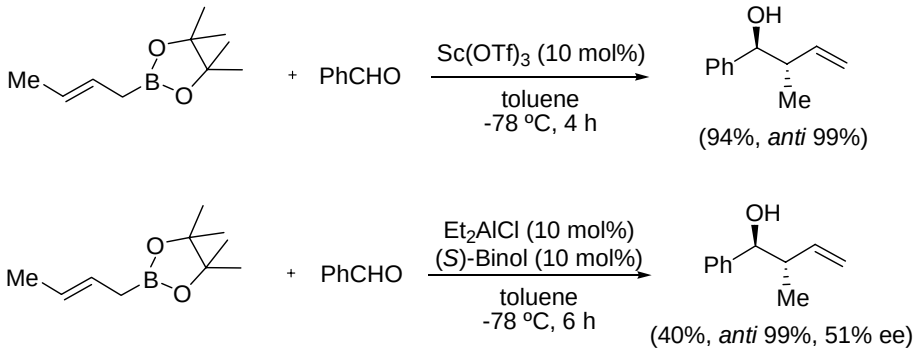
Recently, the Lewis acid catalyzed activation of allylboronates was proposed,[122] and the stereoespecificity observed in the thermal reaction is preserved under this new catalytic approach. Because of the self-activation mechanism of the reaction in the thermal conditions, the use of an external promoting agent would appear to be no advantage. Furthermore, an external Lewis acid might compete with the boron atom for the aldehyde and by this way following a less selective open-chain mechanism. However, Hall and coworkers showed a rate enhancement by a Lewis acid in the allylation reaction[123] and on the basis of experiments and kinetic studies, proposed a chair-like bimolecular transition structure similar to the thermal additions for this electrophilic boronate activation mechanism (*Scheme XXIII*).[124] The catalytic effect is thought to derive from an increase in the electrophilicity of the boron atom following binding of the metal ion to one of the boronate oxygens (**XXVII**) as opposed to coordination of the carbonyl oxygen (**XXVIII**). Thus, coordination of the Lewis acid to the boronate oxygens would disrupt the overlap of the oxygen lone pairs with the empty *p*-orbital of the boron atom. Consequently, the boron center is rendered more electron deficient, and compensates by strengthening the key boron-carbonyl interaction and, concomitantly, lowering the activation energy of the reaction.



Scheme XXIII. *Possible transition structures for the Lewis acid (L.A.) catalyzed allylboration (X = CO_2R'' or noncoordinated H).*

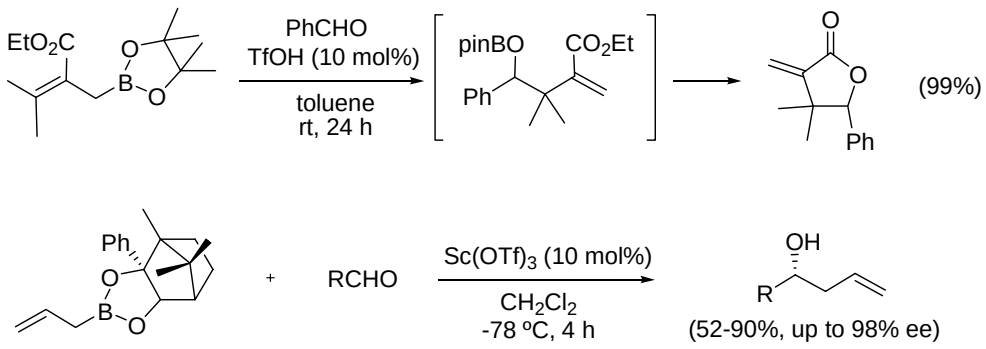
[122] (a) Hall, D. G. *Synlett* **2007**, 1644-1655. (b) Carosi, L.; Lachance, H.; Hall, D. G. *Tetrahedron* **2005**, *46*, 8981-8985.
[123] (a) Kennedy, J. W. J.; Hall, D. G. *Angew. Chem., Int. Ed.* **2003**, *42*, 4732-4739. (b) Kennedy, J. W. J.; Hall, D. G. *J. Org. Chem.* **2004**, *69*, 4412-4428.
[124] Rauniyar, V.; Hall, D. G. *J. Am. Chem. Soc.* **2004**, *126*, 4518-4519.

Miyaura and coworkers showed the first example of catalytic allylboration with moderated enantioselectivity in a greatly accelerated reaction catalyzed by a Lewis acid such as $AlCl_3$ and $Sc(OTf)_3$ combined with a chiral inductor at -78 °C, while the reaction does not proceed in the absence of a Lewis acid (*Scheme XXIV*).[125] This reaction have been supported by a quantum chemical study.[126]



Scheme XXIV.*Lewis acid catalyzed allylboration* .

More recently, Brønsted acid catalysts (i.e. triflic acid) have been also developed even with deactivated allylboronates and aldehydes (*Scheme XXV*).[127]



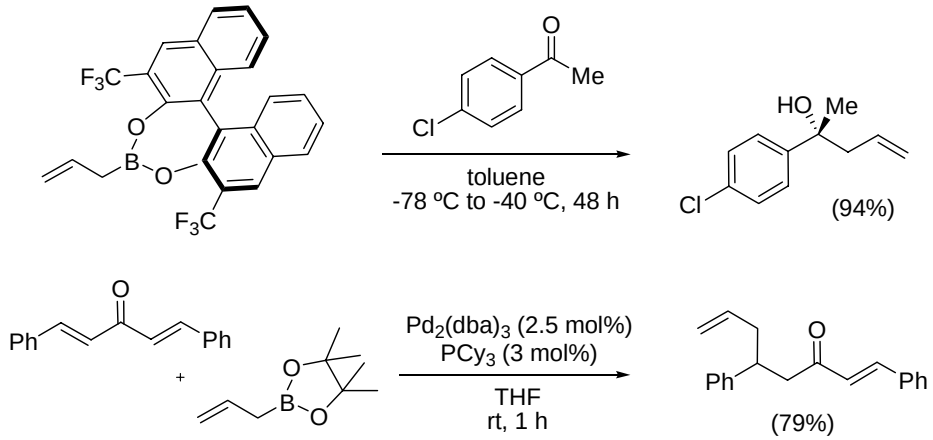
Scheme XXV. *Brønsted and Lewis acid catalyzed allylboration.*

In order to improve the control of the absolute stereoselectivity in this allylation reactions, two new strategies have been applied: (a) development of allylboronates with an α-chiral carbon,[128] or (b) allylboronates with a chiral unit on the boron's two

[125] Ishiyama, T.; Ahiko, T.; Miyaura, N. *J. Am. Chem. Soc.* **2002**, *124*, 12414-12415.
[126] Sakata, K.; Fujimoto, H. *J. Am. Chem. Soc.* **2008**, *130*, 12519-12526.
[127] (a) Elford, T. G.; Arimura, Y.; Yu, S. H.; Hall, D. G. *J. Org. Chem.* **2007**, *72*, 1276-1284. (b) Rauniyar, V.; Zhai, H.; Hall, D. G. *J. Am. Chem. Soc.* **2008**, *130*, 8481-8490.
[128] Stürmer, R.; Hoffmann, R. W; *Synlett* **1990**, 759-761.

heteroatom substituents (*Scheme XXV*),[129] being the last currently more popular because it is generally easier to modify. By this way, excellent levels of stereocontrol have been achieved.

Finally, not only aldehydes have been subjected to this reaction, other electrophilic partners such as ketones[130] and imine derivatives[131] carry out the allylation yielding tertiary homoallylic alcohols and amines, respectively. Moreover, catalytic conjugate addition of allylboronates to activated enones has been reported by Morken and coworkers using Pd or Ni and electron-rich phosphines ligands (*Scheme XXVI*).[132]



Scheme XXVI. *Allylboration of ketones.*

1.4.2.3 Other C–C and C–Heteroatom Bond Forming Reactions

Boronic acid derivatives are also involved in other important C-C and even C-heteroatom bond forming reactions. Next, a brief general introduction of each will be commented.

- **Uncatalyzed Additions to Imines and Iminiums**

The first example of an addition reaction of an Csp^2–B based organoboronic acid to an iminium ion was reported in 1993,[133] when the addition of (*E*)-alkenylboronic acids to preformed iminium ions derived from secondary amines and formaldehyde generating

[129] Lachance, H.; Lu, X.; Gravel, M.; Hall, D. G. *J. Am. Chem. Soc.* **2003**, *125*, 10160-10161.
[130] Wu, T. R.; Shen, L.; Chong, J. M. *Org. Lett.* **2004**, *6*, 2701-2704.
[131] Sebelius, S.; Wallner, O. A.; Szabó, K. J. *Org. Lett.* **2003**, *5*, 3065-3068.
[132] Sieber, J. D.; Liu, S.; Morken, J. P. *J. Am. Chem. Soc.* **2007**, *129*, 2214-2215.
[133] Petasis, N. A.; Akritopolou, I. *Tetrahedron Lett.* **1993**, *34*, 583-586.

allylic amines was demostrated. Later, in 1997, Petasis described a novel uncatalyzed three-component reaction between α-ketoacids, amines and boronic acids, providing a novel synthetic route to α-amino acids. [134] Moreover, the use of α-hydroxyaldehydes lends access to β-aminoalcohols in high yields and excellent stereoselectivity.[135]
This interesting synthetic reaction works with aryl, alkynyl and alkenylboronic acids and esters with a wide range of amines (dialkyl, acyclic or cyclic) and carbonyl derivatives. The reaction is better known as "Petasis borono-Mannich" reaction among others (*Scheme XXVII, green*).

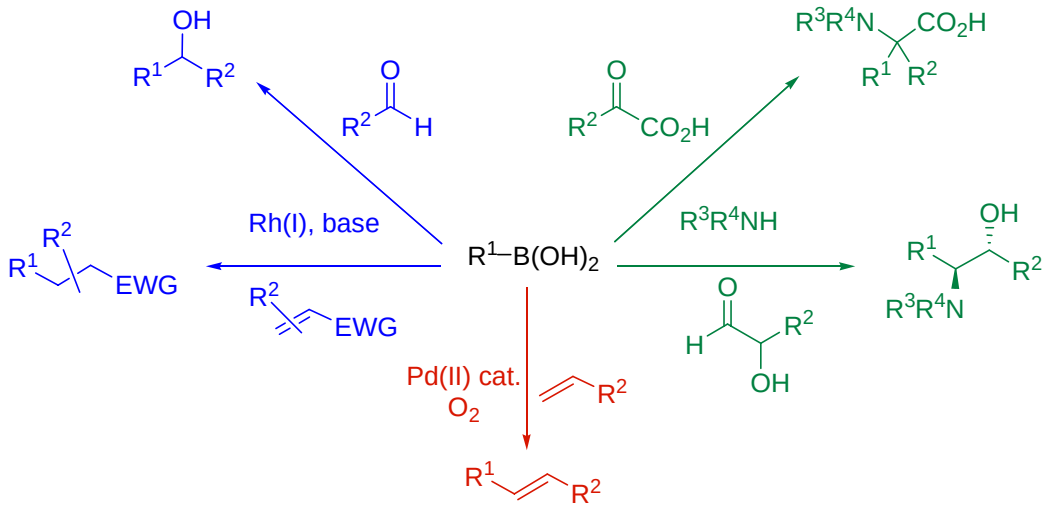
- **Rh-Catalyzed Additions to Aldehydes and Alkenes**

Another interesting process is the addition of boronic acids to carbonyl compounds[5] and a wide range of alkene substrates[4] catalyzed by Rh(I) complexes (*Scheme XXVII, blue*). This latter process can even provide enantioselectivities over 99% in 1,4-additions to enones.[136]
Furthermore, Pd and Ni catalysts promote similar additions of boronic acids onto unactivated insaturated and poliinsaturated compounds.[137]

- **Heck-Type Coupling to Alkenes and Alkynes**

Boronic acids have the ability to undergo addition-dehydrogenation reactions on alkenes in catalyzed processes by transition metals such as Rh, Ru, Ir and Pd (*Scheme XXVII, red*).[138] In addition, similar processes have been describe for alkynes.[139]

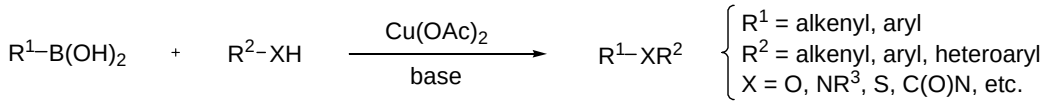
[4] Sakai, M.; Hayashi, H.; Miyaura, N. *Organometallics* **1997**, *16*, 4229-4231.
[5] Sakai, M.; Ueda, M.; Miyaura, N. *Angew. Chem., Int. Ed.* **1998**, *37*, 3279-3281.
[134] Petasis, N. A.; Zavialov, I. A. *J. Am. Chem. Soc.* **1997**, *119*, 445-446.
[135] Petasis, N. A.; Zavialov, I. A. *J. Am. Chem. Soc.* **1998**, *120*, 11798-11799.
[136] Hayashi, T.; Yamasaki, K. *Chem. Rev.* **2003**, *103*, 2829-2844.
[137] With alkynes: (a) Oh, C. H.; Jung, H. H.; Kim, K. S.; Kim, N. *Angew. Chem., Int. Ed.* **2003**, *42*, 805-808. With allenes: (b) Oh, C. H.; Ahn, T. W.; Reddy, R. *Chem. Commun.* **2003**, 2622-2623. With 1,3-butadienes: (c) Shirakawa, E.; Takahashi, G.; Tsuchimoto, T.; Kawakami, Y. *Chem. Commun.* **2002**, 2210-2211.
[138] For Rh: (a) Zou, G.; Wang, Z.; Zhu, J.; Tang, J. *Chem. Commun.* **2003**, 2438-2439. For Ru: (b) Farrington, E. J.; Brown, J. M.; Barnard, C. F. J.; Rowsell, E. *Angew. Chem., Int. Ed.* **2002**, *41*, 169-171. For Ir: (c) Koike, T.; Du, X.; Sanada, T.; Danda, Y.; Mori, A. *Angew. Chem., Int. Ed.* **2003**, *42*, 89-92. For Pd: (d) Jung, Y. C.; Mishra, R. K.; Yoon, C. H.; Jung, K. W. *Org. Lett.* **2003**, *5*, 2231-2234.
[139] Zou, G.; Zhu, J.; Tang, J. *Tetrahedron Lett.* **2003**, *44*, 8709-9711.



Scheme XXVII. *Other C-C bond forming reactions.*

• Cu-Catalyzed Coupling with Nucleophilic Heteroatom-Containing Compounds

One of the most important breakthroughs in the application of boronic acids to organic syntheis is the development of a C–heteroatom (C–X, where X = O, N, S) bond forming reaction, analogous to the Suzuki coupling, to allow the preparation of compounds such as aryl ethers, anilines or aryl thioethers in mild conditions (*Scheme XXVIII)*.[140] In this respect, improvements of the Cu(II)-promoted coupling of aryl and heteroaryl boronic acids to moderately acidic heteroatom-containing functionalities must be considered.[141] The mechanistic pathway suggested is based on transmetallation of the boronic acid with $Cu(OAc)_2$ followed by ligand exchange with the nucleophilic substrate, and finally reductive elimination to give the coupling product.



Scheme XXVIII. *General Cu-catalyzed C-heteroatom bond forming reaction.*

[140] Chan, D. M. T.; Monaco, K. L.; Wang, R.-P.; Winters, M. P. *Tetrahedron Lett.* **1998**, *39*, 2933-2936.
[141] Ley, S. V.; Thomas, A. W. *Angew. Chem., Int. Ed.* **2003**, *42*, 5400-5449.

2. Transition Metal-Catalyzed Enyne Cyclization

The development of new cyclization reactions starting from simple acyclic materials is an important goal in organic synthesis. The use of transition metals as catalysts improves the existing uncatalyzed cyclization reactions and allows the development of new types of reactivity.[142] Depending on the functional groups and the experimental conditions, several transformations are possible which lead to cyclic derivatives. In particular, transition metals catalyzed the cyclization of 1,n-enynes affording highly functionalized carbo- and heterocycles.[142e,143] Apart from the intrinsic rearrangements of 1,n-enynes, several tandem reactions incorporating intramolecular trapping agents or intermolecular partners allow the construction of more complex organic species.[144] These transformations usually proceed with high levels of atom economy[145] and selectivity and in many cases are convenient to perform even on a large scale.

Stoichiometric reactions of enynes promoted by a variety of transition metal complexes, such us Ti, Zr, Co, Ni, Fe or Zn have also been described.[146] However, the catalytic versions are synthetically more useful, and this introduction will focus on this type of transformations, with special attention to Pd systems.

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[142] (a) Negishi, E. *Comprenhensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon: Oxford, 1991; Vol 5, pp 1163-1184. (b) Tamao, K.; Kobayashi, K.; Ito, Y. *Synlett* **1992**, 539-546. (c) Lautens, M.; Klute, W.; Tam, W. *Chem. Rev.* **1996**, *96*, 49-92. (d) Ojima, I.; Tzamarioudaki, M.; Li, Z.; Donovan, R. J. *Chem. Rev.* **1996**, *96*, 635-662. (e) Nakamura, I.; Yamamoto, Y. *Chem. Rev.* **2004**, *104*, 2127-2198. (f) Schore, N. E. *Chem. Rev.* **1998**, *88*, 1081-1119. (g) Frühauf, H.-W. *Chem. Rev.* **1997**, *97*, 523-596.

[143] (a) Negishi, E.; Copéret, C.; Ma, S.; Liou, S.-Y.; Liu, F. *Chem. Rev.* **1996**, *96*, 365-393. (b) Trost, B. M.; Toste, D. F.; Pinkerton, A. B. *Chem. Rev.* **2001**, *101*, 2067-2096. (c) Aubert, C.; Buisine, O.; Malacria, M. *Chem. Rev.* **2002**, *102*, 813-834. (d) Lloyd-Jones, G. C. *Org. Biomol. Chem.* **2003**, *1*, 215-236. (e) Echavarren, A. M.; Nevado, C. *Chem. Soc. Rev.* **2004**, *33*, 431-436. (f) Zhang, L.; Sun, J.; Kozmin, S. A. *Adv. Synth. Catal.* **2006**, *348*, 2271-2296. (g) Michelet, V.; Toullec, P. Y.; Genêt, J.-P. *Angew. Chem., Int. Ed.* **2008**, *47*, 2-50.

[144] (a) Denmark, S. E.; Thorarensen, A. *Chem. Rev.* **1996**, *96*, 137-166. (b) Malacria, M. *Chem. Rev.* **1996**, *96*, 289-306. (c) Tietze, L. F.; Haunert, F. In *Stimulating Concepts in Chemistry*; Vögtle, F.; Stoddart, J. F.; Shibasaki, M., Eds.;Wiley VCH: Weinheim, Germany, 2000, pp 39-64. (d) Chapman, C. J.; Frost, C. G. *Synthesis* **2007**, 1-21.

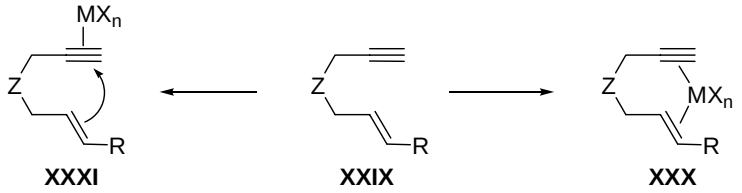
[145] (a) Trost, B. M. *Science* **1991**, *254*, 1471-1477. (b) Trost, B. M. *Acc. Chem. Res.* **2002**, *35*, 695-705.

[146] Ti: (a) Takayama, Y.; Gao, Y.; Sato, F. *Angew. Chem., Int. Ed.* **1997**, *36*, 851-853. (b) Urabe, H.; Suzuki, K.; Sato, F. *J. Am. Chem. Soc.* **1997**, *119*, 10014-10027. (c) Urabe, H.; Sato, F. *J. Am. Chem. Soc.* **1999**, *121*, 1245-1255. (d) Takayama, Y.; Okamoto, S.; Sato, F. *J. Am. Chem. Soc.* **1999**, *121*, 3559-3560. (e) Sato, F.; Urabe, H.; Okamoto, S. *Synlett* **2000**, 753-775. (f) Nakajama, R.; Urabe, H.; Sato, F. *Chem. Lett.* **2002**, *31*, 4-6. Zr: (g) Pagenkopf, B. L.; Lund, E. C.; Livinghouse, T. *Tetrahedron* **1995**, *51*, 4421-4438. (h) Miura, K.; Funatsu, M.; Saito, H.; Ito, H.; Hosomi, A. *Tetrahedron Lett.* **1996**, *37*, 9059-9062. Co: (i) Buisine, O.; Aubert, C.; Malacria, M. *Chem. Eur. J.* **2001**, *7*, 3517-3525, and references therein. Ni: (j) Chowdhury, S. K.; Amarasinghe, K. K. D.; Heeg, M. J.; Montgomery, J. *J. Am. Chem. Soc.* **2000**, *122*, 6775-6776. (k) Chowdhury, S. K.; Amarasinghe, K. K. D.; Heeg, M. J.; Montgomery, J. *Organometallics* **2001**, *20*, 370-372. Fe or Zn: (l) Yamazaki, S.; Yamada, K.; Yamamoto, K. *Org. Biomol. Chem.* **2004**, *2*, 257-264.

Two major pathways can be distinguished in the cyclization of an enyne (**XXIX**) depending on the coordination of the metal (*Scheme XXIX*):

a) If the metal coordinate both moieties, the alkene and the alkyne complex is obtained (**XXX**).

b) If the metal coordinate only to the alkyne (**XXXI**), a nucleophilic attack by the alkene can take place.

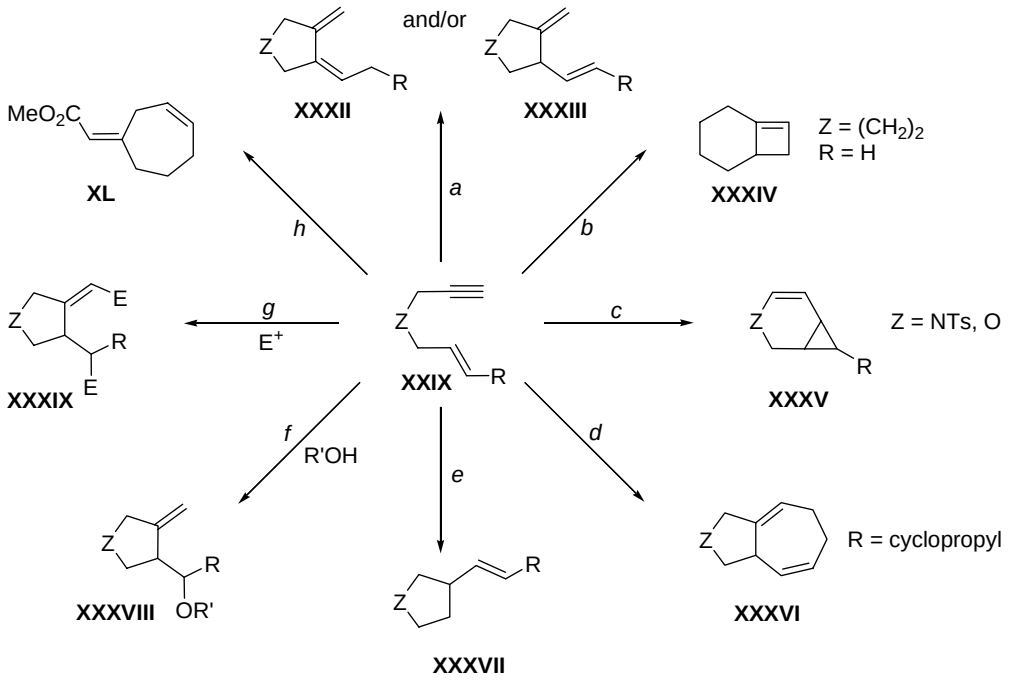


Scheme XXIX. *Coordination pathways.*

Both complexes can lead to transformations known as cycloisomerizations. A cycloisomerization reaction is defined as a reaction in which a section of carbon or carbon–heteroatom chain, which is insaturated at two positions, is isomerized, generating one or more ring systems with concomitant loss of one or more of the insaturations, and without (formal) loss or gain of any atoms.[143d] Since the initial discovery of the Pd-catalyzed Alder-ene reaction by the research group of Trost in 1984,[147] extensive studies on a variety of catalysts and substrates have led to a large array of cycloisomerizations or tandem addition/cycloisomerization transformations (*Scheme XXX*). Thus enynes **XXIX** react in the presence of different metals to give several types of carbo- and heterocyclic products: (a) cyclopentane dienes **XXXII** and/or **XXXIII**,[148,149] (b) bicyclo[4.2.0]octene derivatives **XXXIV**,[150] (c)

[143] (d) Lloyd-Jones, G. C. *Org. Biomol. Chem.* **2003**, *1*, 215-236.
[147] Trost, B. M.; Lautens, M.; Hung, M. H.; Carmichael, C. S. *J. Am. Chem. Soc.* **1984**, *106*, 7641-7643.
[148] Cycloisomerization with Pd: (a) Trost, B. M.; Lautens, M. *J. Am. Chem. Soc.* **1985**, *107*, 1781-1783. (b) Trost, B. M.; Lautens, M. *Tetrahedron Lett.* **1985**, *26*, 4887-4890. (c) Trost, B. M.; Chen, S. -F. *J. Am. Chem. Soc.* **1986**, *108*, 6053-6054. (d) Trost, B. M.; Lautens, M.; Chan, C.; Jebaratnam, D. S.; Mueller, T. *J. Am. Chem. Soc.* **1991**, *113*, 636-644. (e) Trost, B. M.; Gelling, O. J. *Tetrahedron Lett.* **1993**, *34*, 8233-8236. (f) Wartenberg, F. -H.; Hellendahl, B.; Blechert, S. *Synlett* **1993**, 539-540.
[149] Cycloisomerization with other metals, Ru: (a) Paih, J. L.; Rodriguez, D. C.; Dérien, S.; Dixneuf, P. H. *Synlett* **2000**, 95-97. Rh: (b) Cao, P.; Wang, B.; Zhang, X. *J. Am. Chem. Soc.* **2000**, *122*, 6490-6491. (c) Cao, P.; Zhang, X. *Angew. Chem., Int. Ed.* **2000**, *39*, 4104-4106. Pt: (d) Méndez, M.; Muñoz, M. P.; Echavarren, A. M. *J. Am. Chem. Soc.* **2000**, *122*, 11549-11550. (e) Méndez, M.; Muñoz, M. P.; Nevado, C.; Cárdenas, D. J.; Echavarren, A. M. *J. Am. Chem. Soc.* **2001**, *123*, 10511-10520. (f) Muñoz, M. P.; Méndez, M.; Nevado, C.; Cárdenas, D. J.; Echavarren, A. M. *Synthesis* **2003**, 2898-2902.
[150] Trost, B. M.; Yanai, M.; Hoogsteen, K. *J. Am. Chem. Soc.* **1993**, *115*, 5294-5295.

bicyclo[4.1.0]heptene derivatives **XXXV**,[151] (d) fused seven membered ring cycloalkenes (**XXXVI**),[152] (e) vinylcycloalkenes via skeletal reorganization (**XXXVII**),[153] (f) alkoxycyclopentane derivatives containing an *exo* double bond (**XXXVIII**)[149d-f,154] (g) cyclopentane derivatives with an *exo* double bond (**XXXIX**),[155] and (h) seven membered rings (**XL**).[156]



Scheme XXX. *Transition metal-catalyzed cycloisomerizations and related reactions.*

[149] (d) Méndez, M.; Muñoz, M. P.; Echavarren, A. M. *J. Am. Chem. Soc.* **2000**, *122*, 11549-11550. (e) Méndez, M.; Muñoz, M. P.; Nevado, C.; Cárdenas, D. J.; Echavarren, A. M. *J. Am. Chem. Soc.* **2001**, *123*, 10511-10520. (f) Muñoz, M. P.; Méndez, M.; Nevado, C.; Cárdenas, D. J.; Echavarren, A. M. *Synthesis* **2003**, 2898-2902.

[151] (a) Blum, J.; Beer-Kraft, H.; Badrieh, Y. *J. Org. Chem.* **1995**, *60*, 5567-5569. (b) Borodkin, V. S.; Shapiro, N. A.; Azoz, V. A.; Krochetkov, N. K. *Tetrahedron Lett.* **1996**, *37*, 1489-1492. (c) Fürstner, A.; Szillat, H.; Stelzer, F. *J. Am. Chem. Soc.* **2001**, *123*, 11863-11869. (d) Mainetti, E.; Mouries, V.; Fensterbank, L.; Malacria, M. *Angew. Chem., Int. Ed.* **2002**, *41*, 2132-2135.

[152] Rh: (a) Wender, P. A.; Takahashi, H.; Witulski, B. *J. Am. Chem. Soc.* **1995**, *117*, 4720-4721. Ru: (b) Trost. B. M.; Toste, F. D.; Shen, H. *J. Am. Che. Soc.* **2000**, *122*, 2379-2380.

[153] (a) Chatani, N.; Morimoto, T.; Muto, T.; Murai, S. *J. Am. Chem. Soc.* **1994**, *116*, 6049-6050. (b) Chatani, N.; Furukawa. N.; Sakurai, H.; Murai, S. *Organometallics* **1996**, *15*, 901-903. (c) Chatani, N.; Kataoka. K.; Murai, S.; Furukawa, N.; Seki, Y. *J. Am. Chem. Soc.* **1998**, *120*, 9104-9105. (d) Chatani, N.; Inoue, H.; Kotsuma, T.; Murai, S. *J. Am. Chem. Soc.* **2002**, *124*, 10294-10295. (e) Ho-Oh, C.; Youn-Bang, S.; Yun-Rhim, C. *Bull. Korean Chem. Soc.* **2003**, *24*, 887-888.

[154] (a) Nieto-Oberhuber, C.; Muñoz, M. P.; Buñuel, E.; Nevado, C.; Cárdenas, D. J.; Echavarren, A. M. *Angew. Chem., Int. Ed.* **2004**, *43*, 2402-2406. (b) Nieto-Oberhuber, C.; Muñoz, M. P.; López, S.; Jiménez-Nuñez, E.; Nevado, C.; Herrero-Gómez, E.; Raducan, M.; Echavarren, A. M. *Chem. Eur. J.* **2006**, *12*, 1677-1693. (c) Cabello, N.; Rodríguez, C.; Echavarren, A. M. *Synlett* **2007**, 1753-1758. (d) Jiménez-Núñez, E.; Claverie, C. K.; Bour, C; Cárdenas, D. J.; Echavarren, A. M. *Angew. Chem., Int. Ed.* **2008**, *47*, 7892-7895. (e) Bartolom,e, C.; Ramiro, Z.; Pérez-Galán, P.; Bour, C.; Raducan, M.; Echavarren, A. M.; Espinet, P. *Inorg. Chem.* **2008**, *47*, 11391-11397.

[155] Montchamp, J. L.; Neghisi, E. *J. Am. Chem. Soc.* **1998**, *120*, 5345-5346.

[156] Trost, B. M.; Toste, F. D. *J. Am. Chem. Soc.* **2002**, *124*, 5025-5036.

2.1 Alder-Ene-Type Cycloisomerization of Enynes

The Alder-ene reaction is defined as a six electron pericyclic process between an alkene bearing an allylic hydrogen and an electron-deficient multiple bond, which leads to formation of two σ-bonds and migration of the π-bond.[157] The transition metal catalyzed Alder-ene reaction has broadened the applicability of the classic thermal version due to the milder conditions required and the high regio-, stereo- and diastereoselectivity exerted by the metal fragment.

The Alder-ene-type cycloisomerization of enynes has been carried out with complexes of Pd,[148a-d,158,159] Ru,[149a,160] Rh,[149b,161,162] Pt,[143f,149e] Ti,[163] Co,[164] Ir,[165] Ni/Cr,[166] Fe,[167] Ag,[168] and Hg.[169]

[143] (f) Zhang, L.; Sun, J.; Kozmin, S. A. *Adv. Synth. Catal.* **2006**, *348*, 2271-2296.

[148] (a) Trost, B. M.; Lautens, M. *J. Am. Chem. Soc.* **1985**, *107*, 1781-1783. (b) Trost, B. M.; Lautens, M. *Tetrahedron Lett.* **1985**, *26*, 4887-4890. (c) Trost, B. M.; Chen, S. -F. *J. Am. Chem. Soc.* **1986**, *108*, 6053-6054. (d) Trost, B. M.; Lautens, M.; Chan, C.; Jebaratnam, D. S.; Mueller, T. *J. Am. Chem. Soc.* **1991**, *113*, 636-644.

[149] (a) Paih, J. L.; Rodriguez, D. C.; Dérien, S.; Dixneuf, P. H. *Synlett* **2000**, 95-97. (b) Cao, P.; Wang, B.; Zhang, X. *J. Am. Chem. Soc.* **2000**, *122*, 6490-6491. (e) Méndez, M.; Muñoz, M. P.; Nevado, C.; Cárdenas, D. J.; Echavarren, A. M. *J. Am. Chem. Soc.* **2001**, *123*, 10511-10520.

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[159] (a) Trost, B. M.; Lee, D. C.; Rise, F. *Tetrahedron Lett.* **1989**, *30*, 651-654. (b) Trost, B. M.; Shi, Y. *J. Am. Chem. Soc.* **1991**, *133*, 701-703. (c) Trost, B. M.; Pfrengle, W.; Urabe, H.; Dumas, J. *J. Am. Chem. Soc.* **1992**, *114*, 1923-1924. (d) Trost, B. M.; Shi, Y. *J. Am. Chem. Soc.* **1993**, *115*, 9421-9438. (e) Trost, B. M.; Romero, D. L.; Rise, F. *J. Am. Chem. Soc.* **1994**, *116*, 4268-4278. (f) Trost, B. M.; Li, Y. *J. Am. Chem. Soc.* **1996**, *118*, 6625-6633.

[160] (a) Trost, B. M.; Toste, F. D. *J. Am. Chem. Soc.* **1999**, *121*, 9728-9729. (b) Trost, B. M.; Toste, F. D. *J. Am. Chem. Soc.* **2000**, *122*, 714-715. (c) Trost, B. M.; Brown, R. E.; Toste, F. D. *J. Am. Chem. Soc.* **2000**, *122*, 5877-5878. (d) Trost, B. M.; Toste, F. D. *J. Am. Chem. Soc.* **2002**, *124*, 5025-5036. (e) Nishida, M.; Adachi, N.; Onozuka, K.; Matsumura, H.; Mori, M. *J. Org. Chem.* **1998**, *63*, 9158-9159. (f) Trost, B.M.; Surivet, J.-P.; Toste, F. D. *J. Am. Chem. Soc.* **2004**, *126*, 15592-15602. (g) Trost, B. M.; Dong, L.; Schroeder, G. M. *J. Am. Chem. Soc.* **2005**, *127*, 10259-10268.

[161] (a) Grigg, R.; Stevenson, P.; Worakun, T. *Tetrahedron* **1988**, *44*, 4967-4972. (b) Cao, P.; Wang, B.; Zhang, X. *J. Am. Chem. Soc.* **2000**, *122*, 6490-6491. (c) Cao, P.; Zhang, X. *Angew. Chem., Int. Ed.* **2000**, *39*, 4104-4106. (d) Mikami, K.; Kataoka, S.; Aikawa, K. *Org. Lett.* **2005**, *7*, 5777-5780. (e) Nicolaou, K. C.; Edmonds, D. J.; Li, A.; Tria, G. S. *Angew. Chem., Int. Ed.* **2007**, *46*, 3942-3945.

[162] Cycloisomerization with halogen shift, (a) Tong, X.; Zhang, Z.; Zhang, X. *J. Am. Chem. Soc.* **2003**, *125*, 6370-6371. (b) Tong, X.; Li, D.; Zhang, Z.; Zhang, X. *J. Am. Chem. Soc.* **2004**, *126*, 7601-7607.

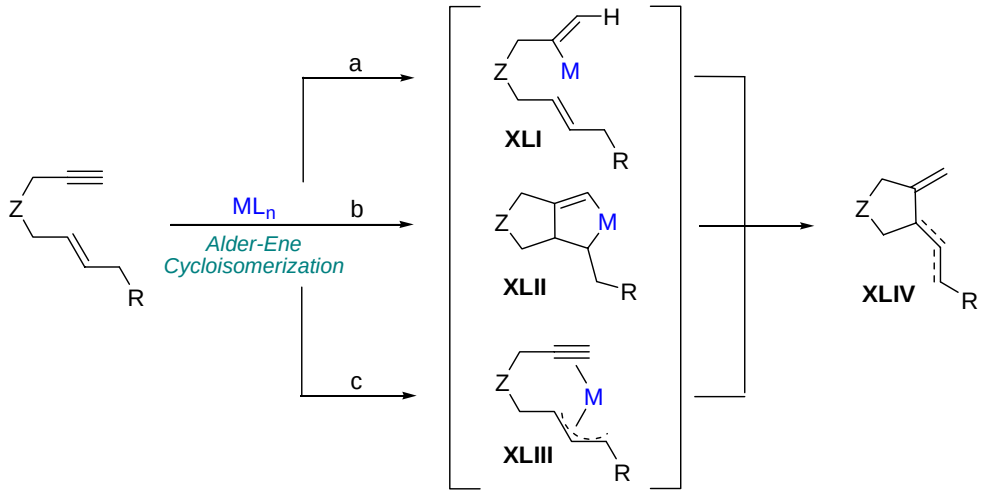
[163] Sturla, S. J.; Kablaoui, N. M.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 1976-1977.

Three major pathways have been proposed for this reaction (*Scheme XXXI*):

(a) Hydrometallation of the alkyne with a M–H species to give the vinylmetal **XLI**.

(b) Oxidative cyclometallation via simultaneous coordination of both insaturations to form a metallacyclopentene **XLII**.

(c) Formation of π-allyl complex from the alkene moiety (**XLIII**), which can further react with the alkyne.



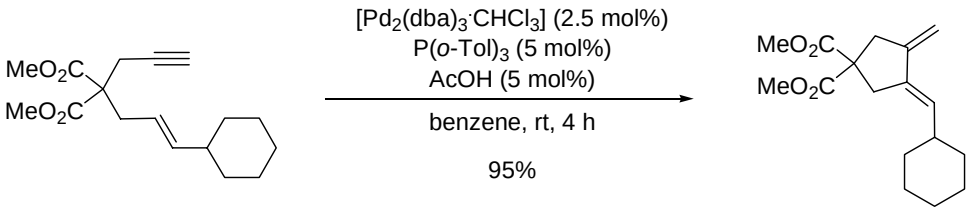
Scheme XXXI. *Transition metal-catalyzed Alder-ene cycloisomerization pathways.*

2.1.1 Alder-Ene-Type Cycloisomerization by a Vinylmetal Pathway

It has been demostrated that the combination of metal complexes in protic or acidic media originates metal hydride species. Trost and coworkers described that Pd(0) species in the presence of a carboxylic acid generate Pd–H species, and this catalytic combination can react with enynes to give the corresponding dienes.[159] The selectivity towards the formation of 1,3- or 1,4-dienes (**XXXII** and **XXXIII**, respectively) depends on steric and electronic factors, but 1,3-dienes are the preferred products in this

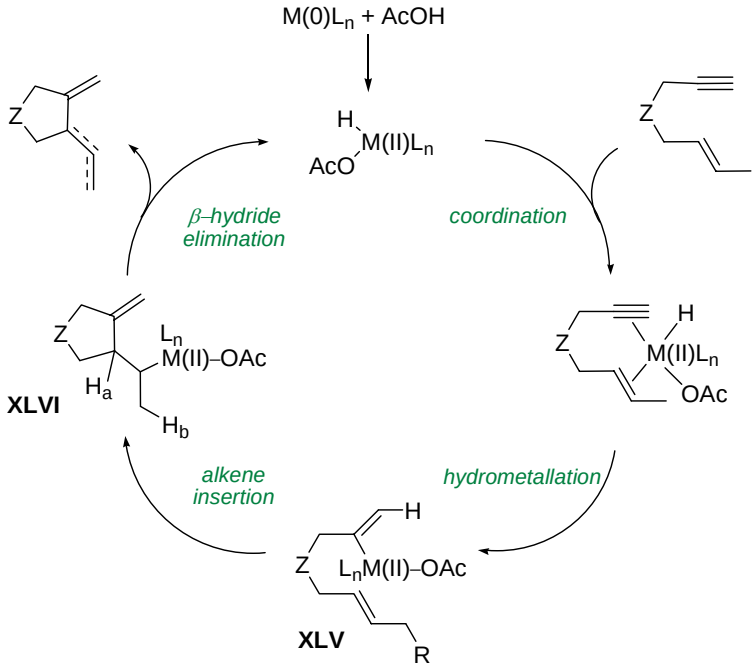
[164] (a) Llerena, D.; Aubert, C.; Malacria, M. *Tetrahedron Lett.* **1996**, *37*, 7353-7356. (b) Buisine, O.; Aubert, C.; Malacria, M. *Chem. Eur. J.* **2001**, *7*, 3517-3525. (c) Ajamian, A.; Gleason, J. L. *Org. Lett.* **2003**, *5*, 2409-2411 and references there in. (d) Chouraqui, G.; Petit, M.; Phansavath, P.; Aubert, C.; Malacria, M. *Eur. J. Org. Chem.* **2006**, 1413-1421.
[165] Chatani, N.; Inoue, H.; Morimoto, T.; Muto, T.; Murai, S. *J. Org. Chem.* **2001**, *66*, 4433-4436.
[166] (a) Trost, B. M.; Tour, J. M. *J. Am. Chem. Soc.* **1987**, *109*, 5268-5270. Ni: (b) Tekavec, T. N.; Louie, J. *Tetrahedron*, **2008**, *64*, 6870–6875. Cr: (c) T. Nishikawa, H. Shinobuko, K. Oshima, *Org. Lett.* **2002**, *4*, 2795-2797.
[167] Fürstner, A.; Martín, R.; Majima, K. *J. Am. Chem. Soc.* **2005**, *127*, 12236-12237.
[168] Harrison, T. J.; Dake, G. R. *Org. Lett.* **2004**, *6*, 5023-5026.
[169] Imagawa, H.; Iyenaga, T.; Nishizawa, M. *Org. Lett.* **2005**, *7*, 451-453.

pathway. Other factors that can determine the regioselectivity are the substitution pattern of the enyne or the nature of the metal ligands (*Scheme XXXII*).



Scheme XXXII. *Formation of an 1,3-diene by a vinylmetal pathway.*

These reactions have shown to proceed by *in situ* generation of a metal hydride, which is the actual catalyst, by oxidative addition of the carboxilic acic to the metal center.[170] The subsequent hydrometallation of the triple bond gives the alkenyl metal complex **XLV**, which suffers 1,2-insertion of the alkene into the M-C bond (intramolecular carbometalation) leading to an alkyl metal complex (**XLVI**). Finally, *β*-hydride elimination from either H_a or H_b gives the 1,3- or 1,4-dienes, respectively, and regenerates the metal hydride species (*Scheme XXXIII*).

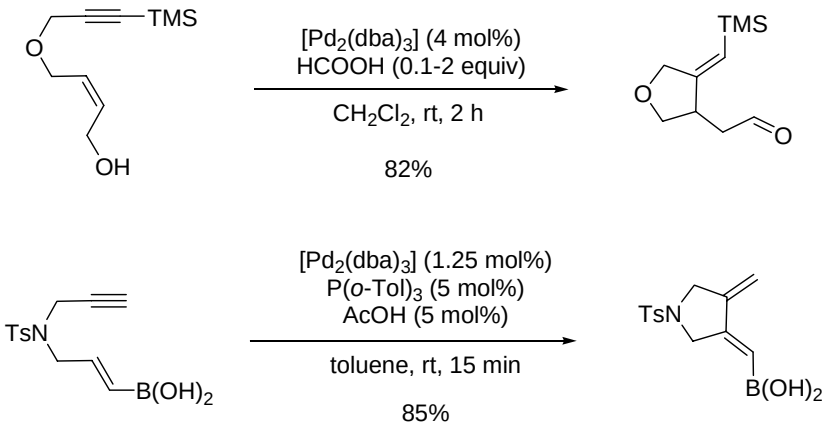


Scheme XXXIII. *Postulated vinylmetal pathway.*

[170] Although no precedent exists for the oxidative addition of acetic acid to Pd(0), stronger acids, such us trifluoroacetic, have been observed to undergo such reactions: (a) Werner, H.; Bertleff, W. *Chem. Ber.* **1983**, *116*, 823-826. (b) Zudin, V. N.; Chinakov, V. D.; Nekipelov, V. M.; Likholobov, V. A.; Ermakov, Y. I. *J. Organomet. Chem.* **1985**, *289*, 425-430.

One of the potential applications of this mechanism is that β-hydride elimination step can be inhibited and the σ-alkylmetal intermediate **XLVI** trapped. Thereby, *one pot* functionalization can be achieved such as reductive cyclization, Stille coupling, tandem cycloisomerizations, etc. These functionalization possibilities will be commented forward.

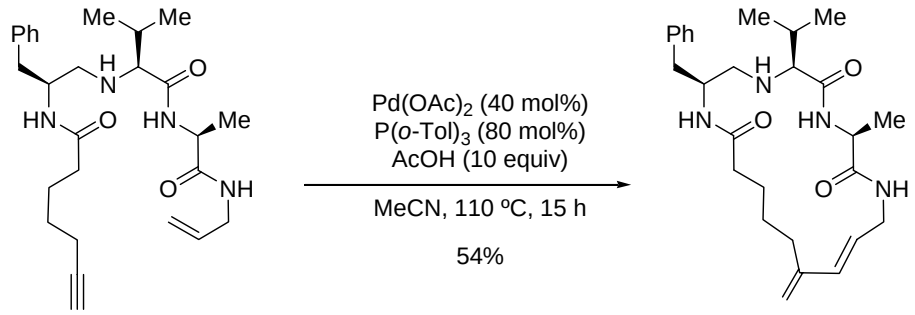
Other possibility of exploiting the Pd-catalyzed cycloisomerization is the *in situ* generation of further reactive groups such as aldehydes[171] or the compatibility of the process with other functional groups (*Scheme XXXIV*).[172] These features allow the preparation, by several known methods, of multicomponent libraries of small organic molecules and make the reaction more appealing.



Scheme XXXIV. *Examples of vinylmetal pathway.*

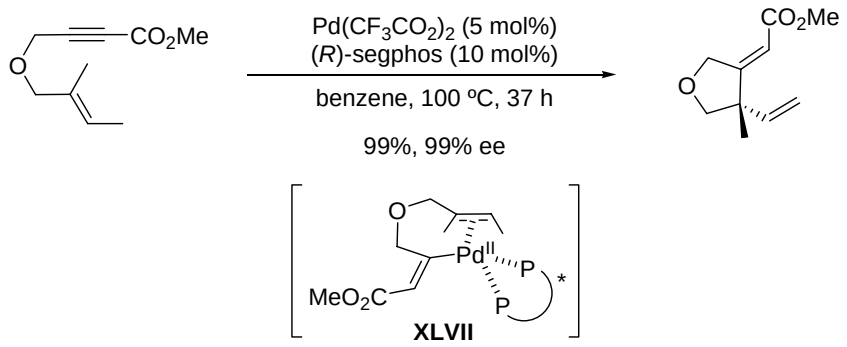
Whereas most studies have focused on the synthesis of five-membered rings starting from 1,6-enynes, the formation of six-membered rings from 1,7-enynes have been also reported.[173] Moreover, this methodology has been applied to the synthesis of macrocyclic compounds (*Scheme XXXV*).[158e,174]

[158] (e) Trost, B. M.; Tanoury, G. J.; Lautens, M.; Chan, C.; MacPherson, D. T. *J. Am. Chem. Soc.* **1994**, *116*, 4255-4267.
[171] Kressierer, C. J.; Müller, T. T. J. *Angew. Chem., Int. Ed.* **2004**, *43*, 5997-6000.
[172] Hercouet, A.; Berrée, F.; Lin, C. H.; Toupet, L.; Carboni, B. *Org. Lett.* **2007**, *9*, 1717-1720.
[173] Trost, B. M.; Li, Y. *J. Am. Chem. Soc.* **1996**, *118*, 6625-6633.
[174] Balraju, V.; Dev, R. V.; Reddy, D. S.; Iqbal, J. *Tetrahedron Lett.* **2006**, *47*, 3569-3571.



Scheme XXXV. *Synthesis of macrocyclic compounds.*

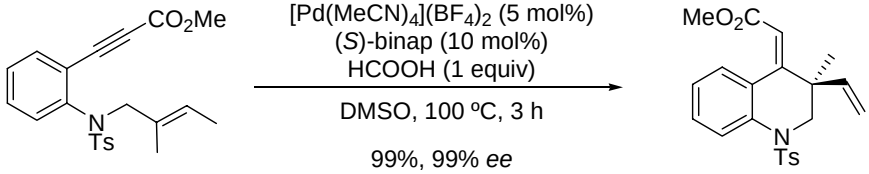
From the last few years, the development of an enantioselective variant of the process has became an important goal in synthetic chemistry.[175] The first highly enantioselective version of this transformations (up to 95%) was reported in 1996 by the research group of Ito,[176] although with low chemoselectivity and limited substrate scope. Later, Mikami and coworkers developed a new Pd-catalytic system based on symmetric bidentate phosphorous ligands affording almost quantitative yields and enantiselectivity of 99% under optimized conditions.[177] The authors favored the formation of a five-coordinate neutral Pd(II) complex (**XLVII**) as the enantiodetermining step (*Scheme XXXVI*). Later, the same group continued the research by using of different catalytic Pd-systems in combination with P and/or N chiral ligands yielding excellent results.[178]



Scheme XXXVI. *Enantioselective version of 1,6-enynes.*

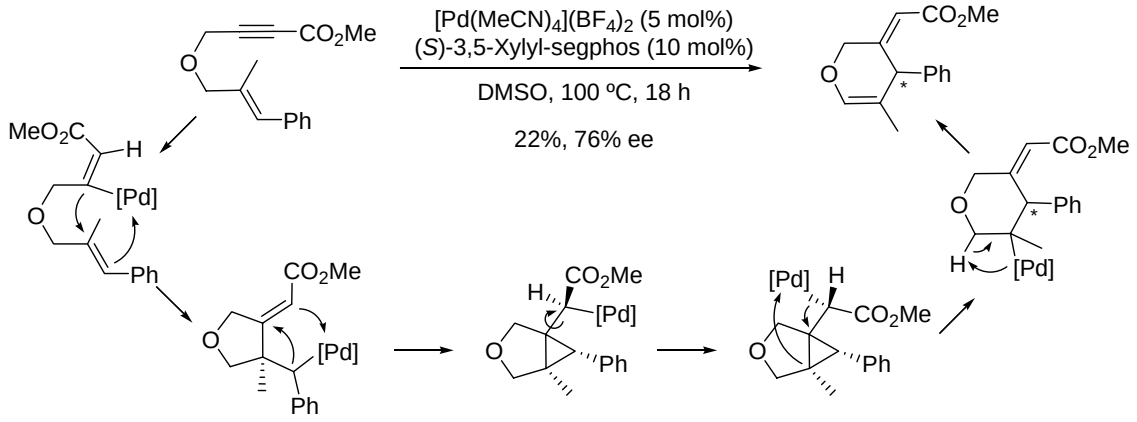
[175] Fairlamb, I. J. S. *Angew. Chem., Int. Ed.* **2004**, *43*, 1048-1052.
[176] Goeke, A.; Sawamura, M.; Kuwano, R.; Ito, Y. *Angew. Chem., Int. Ed.* **1996**, *35*, 662-663.
[177] Hatano, M.; Terada, M.; Mikami, K. *Angew. Chem., Int. Ed.* **2001**, *40*, 249-253.
[178] Hatano, M.; Mikami, K. *Org. Biomol. Chem*. **2003**, *1*, 3871-3873.

Hatano and Mikami extended their study to the asymmetric cycloisomerization of 1,7-enynes (*Scheme XXXVII*).[179]



Scheme XXXVII. *Assymetric version of 1,7-enynes.*

The formation of six-membered ring products from the cyclization of 1,6-enynes have been also reported.[180] The authors proposed a mechanism that involves the hydropalladation of the alkyne giving an alkenyl-Pd, which inserts the alkene. In this insertion, two possibilities can occur: a 5-*exo-trig* or a 6-*endo-trig*. Although both types of cyclization are observed depending upon the catalyst a 5-*exo-trig* cyclization followed by an isomerization via homoallyl-cyclopropyl rearrangement was proposed (*Scheme XXXVIII*).



Scheme XXXVIII. *Six-membered ring formation from 1,6-enynes.*

A similar mechanism, based on carbopalladation instead of hydrometallation, has been proposed in the alkenylative Pd catalyzed cyclization reaction, in the presence of aryl or alkenyl halides.[181]

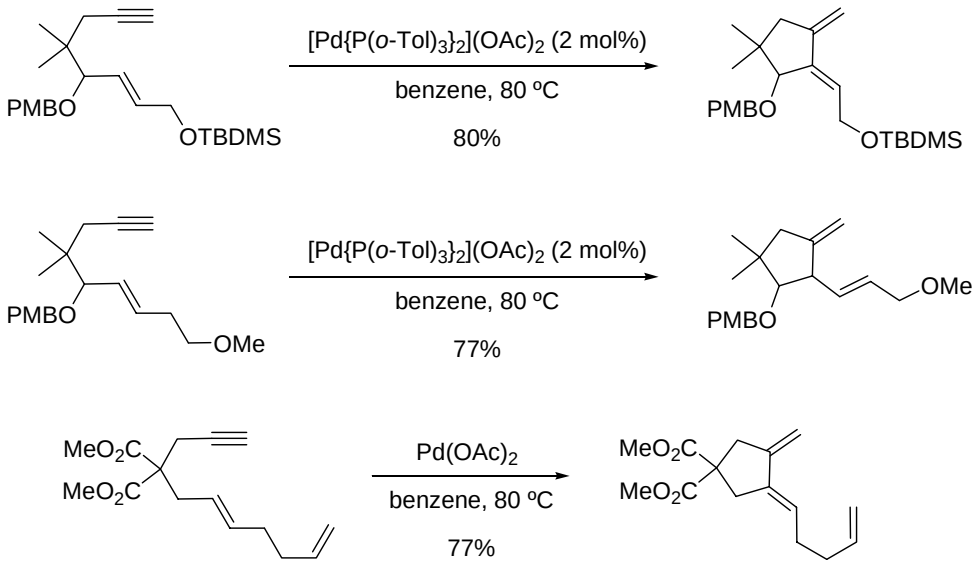
[179] Hatano, M.; Mikami, K. *J. Am. Chem. Soc.* **2003**, *125*, 4704-4705.
[180] (a) Mikami, K.; Hatano, M. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 5767-5769. (b) Yamamoto, Y.; Kuwabara, S.; Ando, Y.; Nagata, H.; Nishiyama, H.; Itoh, K. *J. Org. Chem.* **2004**, *69*, 6697-6705.
[181] Trost, B. M.; Dumas, J. *Tetrahedron Lett.* **1992**, *34*, 19-22.

Finally, other catalytic systems such as Ru(II),[160] Ir(I),[165] Rh(I),[161] and a Ni/Cr-based catalyst system[166] were reported to catalyze this reaction via hydrometallation pathway, being 1,3-dienes the major products. Ni/Zn acid systems has recently also reported to catalyze this reaction, and the same mechanism is proposed to be operative under this conditions, through *in situ* generation of Ni-H species.[182]

2.1.2 Alder-Ene-Type Cycloisomerization by a Metallacyclopentene Pathway

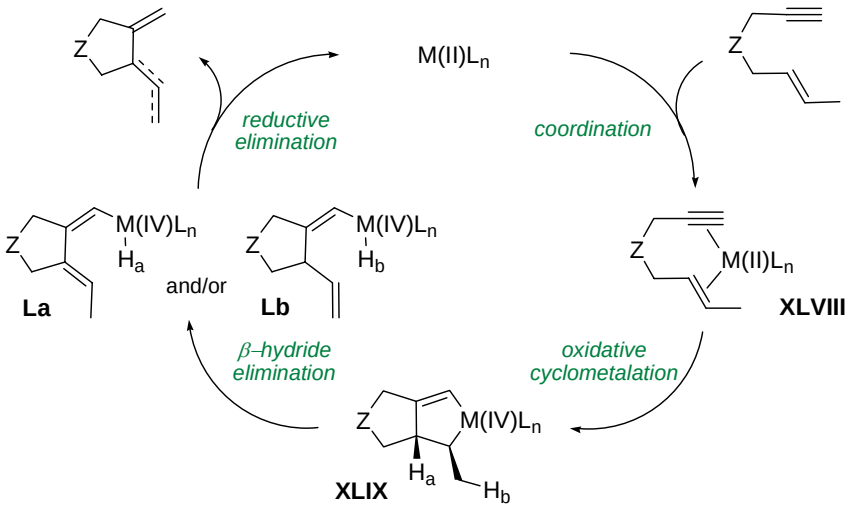
The Alder-ene-type cycloisomerization has also been described by using Pd(II) salts as catalysts, in the presence of appropiate ligands.[158] In this case, substitution at the tether by electron-withdrawing groups facilitates the reaction. As above mentioned, steric and electronic factors influence the regioselectivity of the cyclization. For instance, ether functions are able to influence the regioselectivity of the diene synthesis through their position of attachment in the molecule. Thus, allylic ether leads selectively to 1,3-dienes,[148a,158a] whereas homoallylic ether favors formation of 1,4-dienes (*Scheme XXXIX*).[158e] Moreover, the presence of a remote double bond also favors 1,3-dienes (*Scheme XXXIX*).[158e]

[148] (a) Trost, B. M.; Lautens, M. *J. Am. Chem. Soc.* **1985**, *107*, 1781-1783.
[158] (a) Trost, B. M.; Chung, J. Y. L. *J. Am. Chem. Soc.* **1985**, *107*, 4586-4588. (b) Trost, B. M.; Jebaratnam, D. J. *Tetrahedron Lett.* **1987**, *28*, 1611-1613. (c) Trost, B. M.; Tanoury, G. J. *J. Am. Chem. Soc.* **1987**, *109*, 4753-4755. (d) Trost, B. M.; Phan, L. T. *Tetrahedron Lett.* **1993**, *34*, 4735-4738. (e) Trost, B. M.; Tanoury, G. J.; Lautens, M.; Chan, C.; MacPherson, D. T. *J. Am. Chem. Soc.* **1994**, *116*, 4255-4267. (f) Trost, B. M.; Krische, M. J. *J. Am. Chem. Soc.* **1996**, *118*, 233-234.
[160] (a) Trost, B. M.; Toste, F. D. *J. Am. Chem. Soc.* **1999**, *121*, 9728-9729. (b) Trost, B. M.; Toste, F. D. *J. Am. Chem. Soc.* **2000**, *122*, 714-715. (c) Trost, B. M.; Brown, R. E.; Toste, F. D. *J. Am. Chem. Soc.* **2000**, *122*, 5877-5878. (d) Trost, B. M.; Toste, F. D. *J. Am. Chem. Soc.* **2002**, *124*, 5025-5036. (e) Nishida, M.; Adachi, N.; Onozuka, K.; Matsumura, H.; Mori, M. *J. Org. Chem.* **1998**, *63*, 9158-9159. (f) Trost, B.M.; Surivet, J.-P.; Toste, F. D. *J. Am. Chem. Soc.* **2004**, *126*, 15592-15602. (g) Trost, B. M.; Dong, L.; Schroeder, G. M. *J. Am. Chem. Soc.* **2005**, *127*, 10259-10268.
[161] (a) Grigg, R.; Stevenson, P.; Worakun, T. *Tetrahedron* **1988**, *44*, 4967-4972. (b) Cao, P.; Wang, B.; Zhang, X. *J. Am. Chem. Soc.* **2000**, *122*, 6490-6491. (c) Cao, P.; Zhang, X. *Angew. Chem., Int. Ed.* **2000**, *39*, 4104-4106. (d) Mikami, K.; Kataoka, S.; Aikawa, K. *Org. Lett.* **2005**, *7*, 5777-5780. (e) Nicolaou, K. C.; Edmonds, D. J.; Li, A.; Tria, G. S. *Angew. Chem., Int. Ed.* **2007**, *46*, 3942-3945.
[165] Chatani, N.; Inoue, H.; Morimoto, T.; Muto, T.; Murai, S. *J. Org. Chem.* **2001**, *66*, 4433-4436.
[166] (a) Trost, B. M.; Tour, J. M. *J. Am. Chem. Soc.* **1987**, *109*, 5268-5270. Ni: (b) Tekavec, T. N.; Louie, J. *Tetrahedron*, **2008**, *64*, 6870–6875. Cr: (c) T. Nishikawa, H. Shinobuko, K. Oshima, *Org. Lett.* **2002**, *4*, 2795-2797.
[182] Ikeda, S.; Daimon, N.; Sanuki, R.; Odashima, K. *Chem. Eur. J.* **2006**, *12*, 1794-1806.



Scheme XXXIX. *Regioselectivity on the diene formation by metallacyclopentene pathway.*

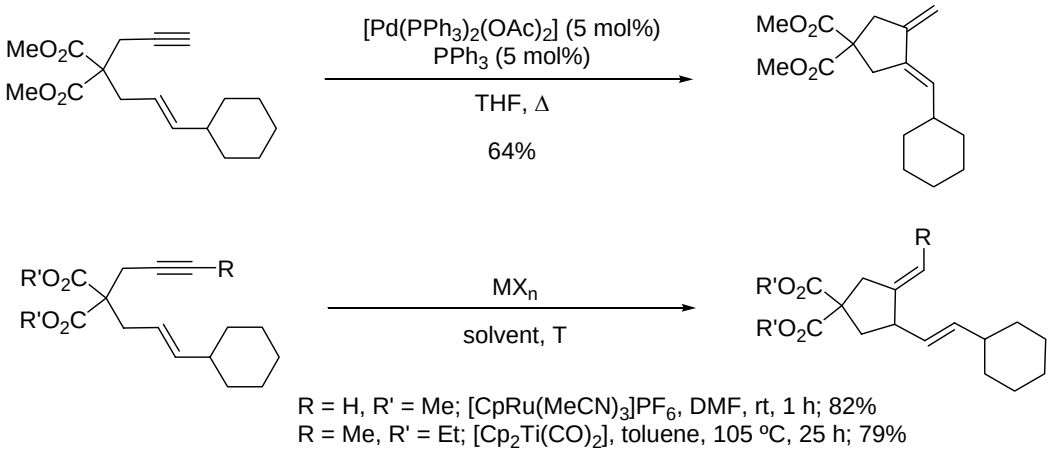
The mechanistic proposal is based on simultaneous coordination of the metal to the alkyne and the alkene **XLVIII**. Then, oxidative cyclometallation leads to the key metallacycle **XLIX**. The *β*-elimination of H_a or H_b gives a vinylmetal complex (**La** or **Lb**), which suffers reductive elimination (*Scheme XL*). The *β*-hydrogen elimination requires a vacant coordination site on the metal and a *cis* disposition of the C-M and the C-H bonds, which have to be aligned to optimize orbital overlap. Due to the conformational restrictions of metallacycle **XLIX**, *β*-hydrogen elimination of H_b is usually more favorable, although elimination of H_a may predominate under certain circumstances.



Scheme XL. *Postulated metallacyclopentene pathway.*

The feasibility of this mechanistic proposal has been studied by DFT calculations in the case of Pt(II).[149e] This study showed that upon coordination of both insaturations (**XLVIII**), oxidative cyclometalation takes place with an E_a = 29.6 kcal mol^{-1} in a process that is exothermic (24.2 kcal mol^{-1}).

Similar reactivity has been observed for Ru(II) cationic complexes.[160] In this system the selectivity towards the diene is complementary to the Pd(II) systems. The same behaviour was observed for the Ti catalyzed reaction described by Buchwald for enynes bearing substituted alkynes and *trans* alkenes (*Scheme XLI*).[163]



Scheme XLI. *Examples of metallacycle pathway.*

The same reactivity was observed with Rh(I)[161b] and Pt(II)[149d-f,183] catalysts to give 1,4-dienes as the main products. Conjugated dienes can be formed in good yields in the thermolysis of the dicobalthexacarbonyl complexes of certain 1,6-enynes (*Scheme XLII*).[184]

[149] (d) Méndez, M.; Muñoz, M. P.; Echavarren, A. M. *J. Am. Chem. Soc.* **2000**, *122*, 11549-11550. (e) Méndez, M.; Muñoz, M. P.; Nevado, C.; Cárdenas, D. J.; Echavarren, A. M. *J. Am. Chem. Soc.* **2001**, *123*, 10511-10520. (f) Muñoz, M. P.; Méndez, M.; Nevado, C.; Cárdenas, D. J.; Echavarren, A. M. *Synthesis* **2003**, 2898-2902.

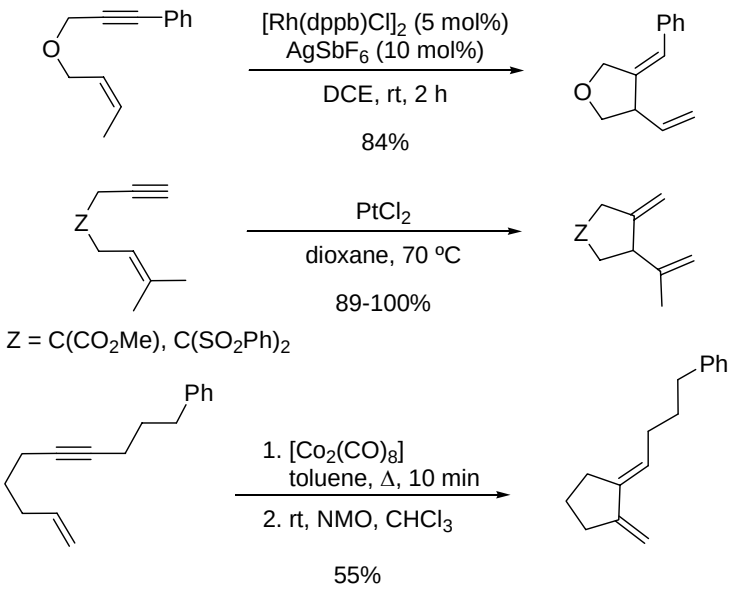
[160] (a) Trost, B. M.; Toste, F. D. *J. Am. Chem. Soc.* **1999**, *121*, 9728-9729. (b) Trost, B. M.; Toste, F. D. *J. Am. Chem. Soc.* **2000**, *122*, 714-715. (c) Trost, B. M.; Brown, R. E.; Toste, F. D. *J. Am. Chem. Soc.* **2000**, *122*, 5877-5878. (d) Trost, B. M.; Toste, F. D. *J. Am. Chem. Soc.* **2002**, *124*, 5025-5036. (e) Nishida, M.; Adachi, N.; Onozuka, K.; Matsumura, H.; Mori, M. *J. Org. Chem.* **1998**, *63*, 9158-9159. (f) Trost, B.M.; Surivet, J.-P.; Toste, F. D. *J. Am. Chem. Soc.* **2004**, *126*, 15592-15602. (g) Trost, B. M.; Dong, L.; Schroeder, G. M. *J. Am. Chem. Soc.* **2005**, *127*, 10259-10268.

[161] (b) Cao, P.; Wang, B.; Zhang, X. *J. Am. Chem. Soc.* **2000**, *122*, 6490-6491.

[163] Sturla, S. J.; Kablaoui, N. M.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 1976-1977.

[183] Harrison, T. J.; Dake, G. R. *Org. Lett.* **2004**, *6*, 5023-5026.

[184] Kraft, M. E.; Wilson, A. M.; Dasse, O. A.; Bonaga, L. V. R.; Cheung, Y. Y.; Fu, Z.; Shao, B.; Scott, I. L. *Tetrahedron Lett.* **1998**, *39*, 5911-5914.



Scheme XLII. *Examples of metallacycle pathway.*

Finally, if an electrophile is present in the reaction mixture, the electrophilic cleavage of the C–M bonds leads to cycles like **XXXIX** (*Scheme XXX*). By this way, carbonylation (Pauson-Khand reaction),[185] hydrolysis or halogenolysis,[186] transmetallation,[155] and addition of carbonyl compounds can also take place.[187]

2.1.3 Alder-Ene-Type Cycloisomerization via π-Allylmetal Pathway

The third mechanistic proposal is based on π-allyl metal complexes, although this is less common. In general, the presence of a leaving group at the allylic position is required to generate the π-allyl moiety.[188,189]

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[155] Montchamp, J. L.; Neghisi, E. *J. Am. Chem. Soc.* **1998**, *120*, 5345-5346.

[185] Reviews on the Pauson-Khand reaction: (a) Pauson, P. L. *Tetrahedron* **1985**, *41*, 5855-5860. (b) Schore, N. E. *Org. React.* **1991**, *41*, 1-90. (c) Schore, N. E. *Comprehensive Organic Synthesis II*; Abel, E. W.; Stone, F. G. A., Wilkinson, G., Hegedus, L., Eds.; Pergamon Press: Oxford, 1995; Vol. 12, pp 703-739. (d) Geis, O.; Schmalz, H. G. *Angew. Chem., Int. Ed.* **1998**, *37*, 911-914. (e) Chung, Y. K. *Coord. Chem. Rev.* **1999**, *188*, 297-341. (f) Brummond, K. M.; Kent, J. L. *Tetrahedron* **2000**, *56*, 3263-3283. (g) Yamanaka, M.; Nakamura, E. *J. Am. Chem. Soc.* **2001**, *123*, 1703-1708. (h) Pericàs, M. A.; Balsells, J.; Castro, J.; Marchueta, I.; Moyano, A.; Riera, A.; Vázquez, J.; Verdaguer, X. *Pure. Appl. Chem.* **2002**, *74*, 167-174. (i) Gibson, S. E.; Stevenazzi, A. *Angew. Chem., Int. Ed.* **2004**, *42*, 1800-1810.

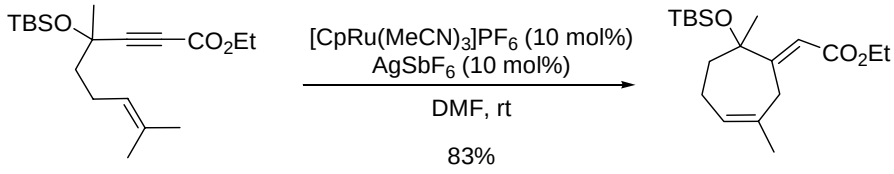
[186] Rajanbabu, T. V.; Nugent, W. A.; Taber, D. F.; Fagan, P. J. *J. Am. Chem. Soc.* **1988**, *110*, 7128-7135.

[187] Copéret, C.; Negishi, E.-I.; Xi, Z.; Takahashi, T. *Tetrahedron Lett.* **1994**, *35*, 695-698.

[188] Holzhapfel, C. W.; Marais, L. *Tetrahedron Lett*. **1998**, *39*, 2179-2182.

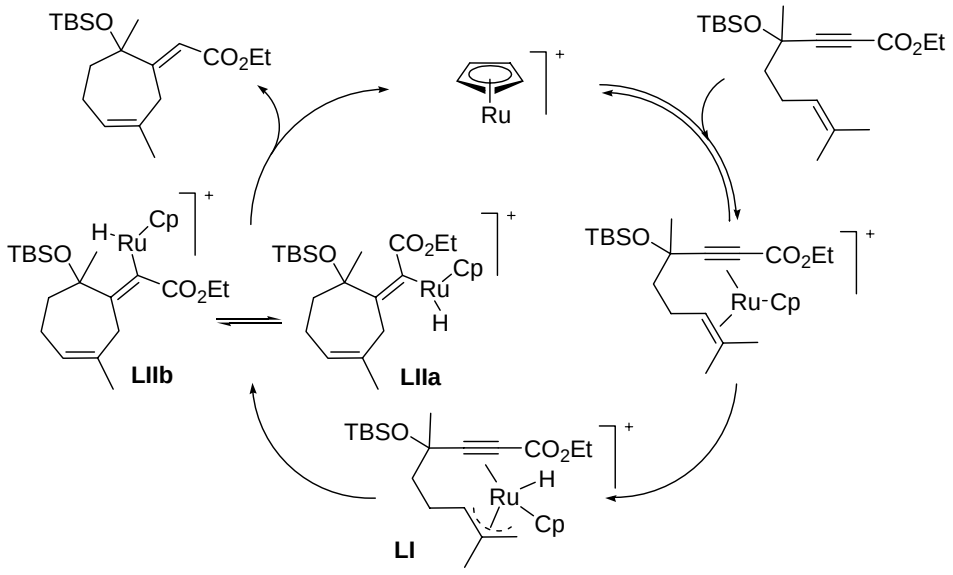
[189] More common is the reaction of π-allyl complexes with alkenes: (a) Oppolzer, W. *Comprehensive Organometallic Chemistry II*; Abel, E. W.; Stone, F. G.; Wilkinson, G.; Hegedus, L., Eds.; Pergamon Elsevier: Oxford, 1995; Vol. 12, pp 905-921. (b) Gómez-Bengoa, E.; Cuerva, J. M.; Echavarren, A. M.; Martorell, G. *Angew. Chem., Int. Ed.* **1997**, *36*, 767-769. (c) Cárdenas, D. J.; Alcamí, M.; Cossío, F.; Méndez, M.; Echavarren, A. M. *Chem. Eur. J.* **2003**, *9*, 96-105.

However, Trost and coworkers have recently described this type of intermediates arising from a C-H activation. This reaction requires a quaternary center at the propargyl position and an acetylenic ester to proceed, and gives rise to the formation of seven-membered rings in good yields (*Scheme XLIII*).



Scheme XLIII. *Allylmetal pathway by C-H bond activation.*

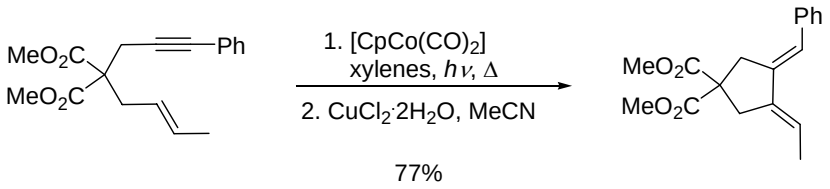
The formation of these products was rationalized by the 1,4-diaxial and 1,3-allylic strain in the ruthenacycle intermediate. The high energy of this intermediate inhibits the metallacyclization and favors activation of the allylic C-H to give π-allylruthenium(IV) hydride **LI** (*Scheme XLIV*). A 7-*exo-dig* carbaruthenation gives vinylruthenium(IV) hydride **LIIa**, which is in equilibrium with **LIIb** via the Ru(IV) allenoate. Reductive elimination occurs selectively from **LIIb** to form the cycloheptene and the Ru(II) catalyst.



Scheme XLIV. *Postulated mechasnism for Ru-catalyzed allylmetal pathway.*

[160] (a) Trost, B. M.; Toste, F. D. *J. Am. Chem. Soc.* **1999**, *121*, 9728-9729. (b) Trost, B. M.; Toste, F. D. *J. Am. Chem. Soc.* **2000**, *122*, 714-715. (c) Trost, B. M.; Brown, R. E.; Toste, F. D. *J. Am. Chem. Soc.* **2000**, *122*, 5877-5878. (d) Trost, B. M.; Toste, F. D. *J. Am. Chem. Soc.* **2002**, *124*, 5025-5036. (e) Nishida, M.; Adachi, N.; Onozuka, K.; Matsumura, H.; Mori, M. *J. Org. Chem.* **1998**, *63*, 9158-9159. (f) Trost, B.M.; Surivet, J.-P.; Toste, F. D. *J. Am. Chem. Soc.* **2004**, *126*, 15592-15602. (g) Trost, B. M.; Dong, L.; Schroeder, G. M. *J. Am. Chem. Soc.* **2005**, *127*, 10259-10268.

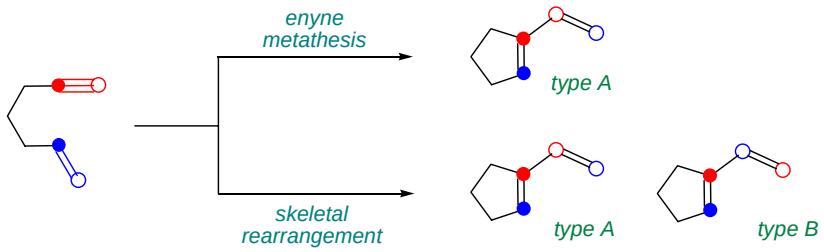
Malacria and coworkers have developed cyclizations of enynes with stoichiometric Co(I).[164a,b] In this case, whatever the length of the tether between the two unsaturated bonds, the cyclization leads only to five membered rings. This reactivity requires the isomerization of the terminal double bond of the starting enyne, probably via oxidative formation of a Co η^3-allyl hydride through a C–H activation process (*Scheme XLV*). Gleason and coworkers have observed similar reactivity on the catalytic version of this reaction.[164c]



Scheme XLV. *Stoichiometric five-membered ring formation.*

2.2 Skeletal Bond Reorganization

When the metal coordinates only to the alkyne, then 1,n-enynes can be cyclized to 1-vinylcycloalkenes by using a variety of transition-metal complexes. This process has been the subject of extensive study, because of its synthetic potential for the construction of carbo- and heterocycles in a single step with full atom economy. Two possible mechanisms, considering the catalyst and the products obtained, have been described for this reaction, enyne metathesys and skeletal rearrangement (*Scheme XLVI*).[190,191]

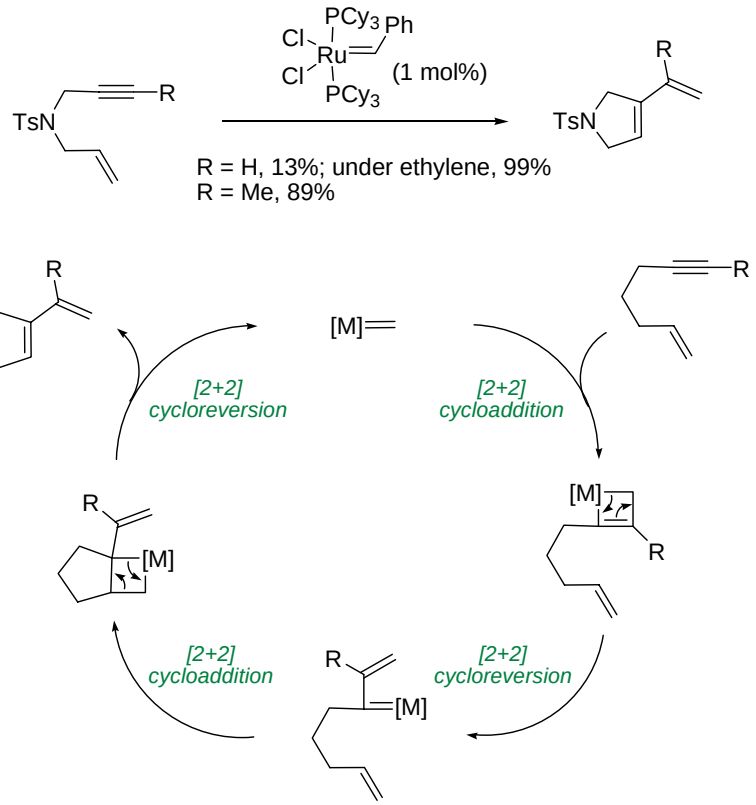


Scheme XLVI. *Possible mechanisms of skeletal bond reorganization.*

[164] (a) Llerena, D.; Aubert, C.; Malacria, M. *Tetrahedron Lett.* **1996**, *37*, 7353-7356. (b) Buisine, O.; Aubert, C.; Malacria, M. *Chem. Eur. J.* **2001**, *7*, 3517-3525. (c) Ajamian, A.; Gleason, J. L. *Org. Lett.* **2003**, *5*, 2409-2411.
[190] Diver, S. T.; Giessert, A. J. *Chem. Rev.* **2004**, *104*, 1317-1382.
[191] Schmidt, B. *Angew. Chem., Int. Ed.* **2003**, *42*, 4996-4999.

• **Enyne metathesis**

Based on the same principles of alkene metathesis, using metal-carbenes as catalyst.[192] The reaction is proposed to proceed through a sequence of [2+2] cycloadditions, and [2+2] cycloreversions. In this case *type A* products (*simple cleavage*), were the carbons of the alkyne remain connected, are obtained (*Scheme XLVII*).



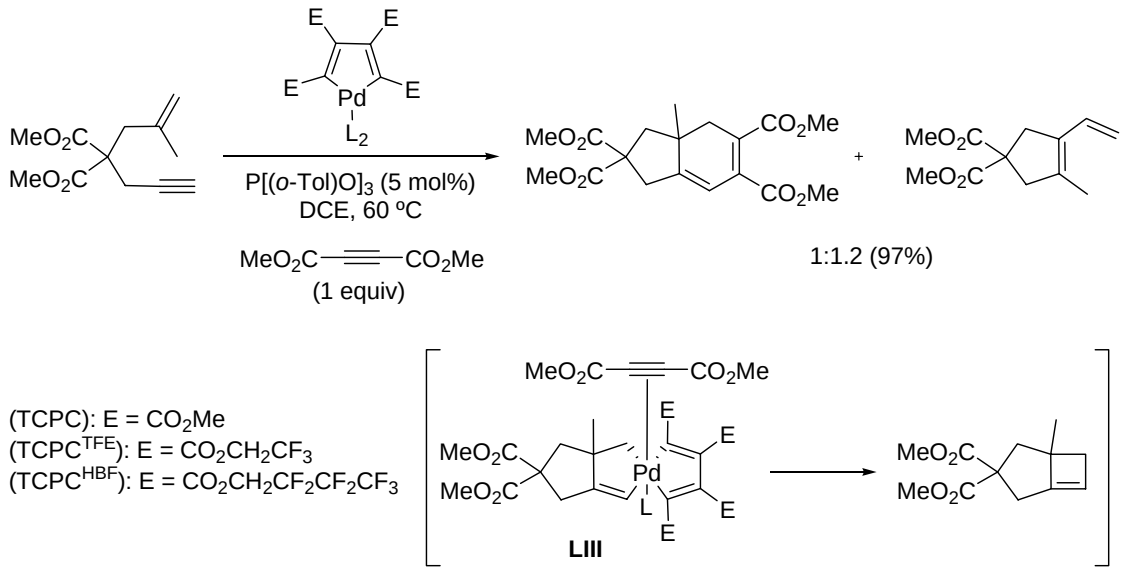
Scheme XLVII. *Plausible mechanism of enyne metathesis.*

• **Skeletal rearrangement of enynes**

Using catalysts that do not possess a carbene ligand (i.e. Pd(II), Pt(II), Pt(IV), Ru(II), Ir(I), Au(I)). Two possible isomers can be obtained, type A (*simple cleavage*), and type B (*double cleavage*), were both insaturations, the alkyne and the alkene, are cleavage.
The first examples of skeletal rearrangement were reported by Trost and Tanoury in 1988,[193] when they carried out the reaction of 1,6-enynes with

[192] (a) Grubbs, R. H. Ed., *Handbook of Metathesis*, Wiley-VCH, **2003**. (b) Connon, S. J.; Blechert, S. *Angew. Chem., Int. Ed.* **2003**, *42*, 1900-1923. (c) N. Dieltiens, K. Moonen, C. V. Stevens, *Chem. Eur. J.* **2007**, *13*, 203 – 214.
[193] Trost, B. M.; Tanoury, G. J. *J. Am. Chem. Soc.* **1988**, *110*, 1636-1638.

tetracarbomethoxypalladacyclopentadiene (TCPC) as catalysts, in the presence of tri-*o*-tolyl phosphite, and one equivalent of dimethyl acetylendicarboxylate (*Scheme XLVIII*). The trifluoroethyl ($TCPC^{TFE}$) and heptafluorobutyl ($TCPC^{HBF}$) derivatives of the catalyst were also used.[194]



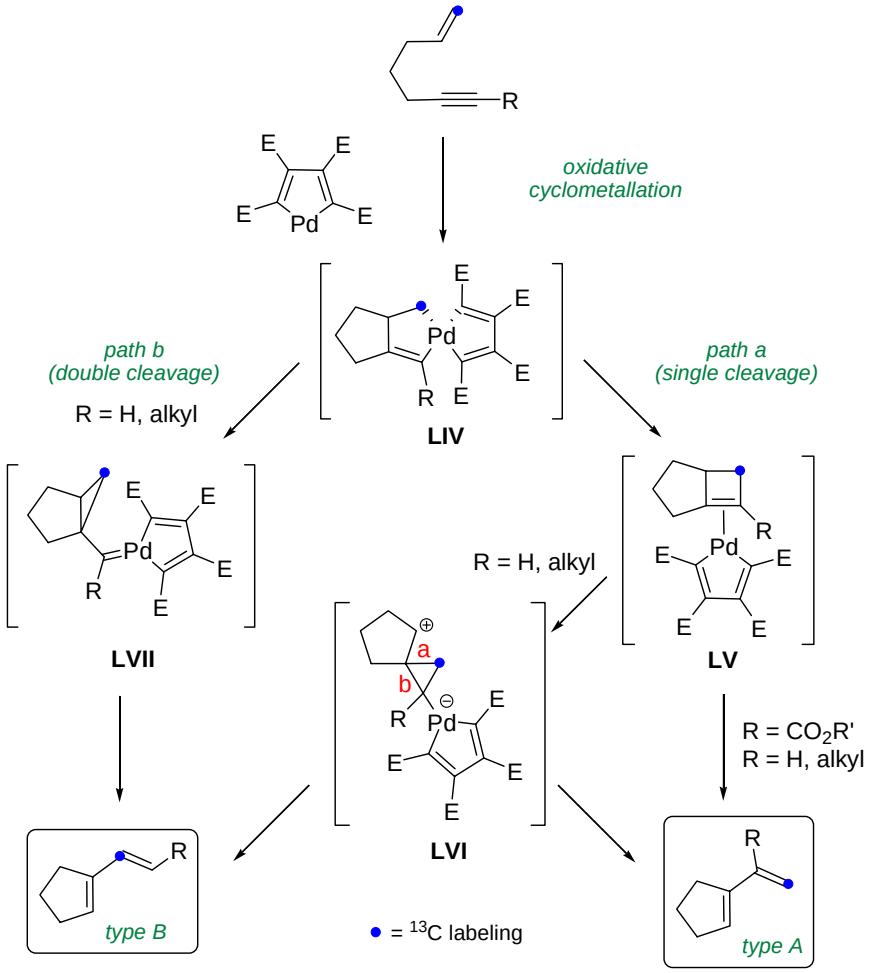
Scheme XLVIII. *Skeletal rearrangement.*

The formation of the vinylcycloalkene (skeletal rearrangement product) was explained via a cyclobutene intermediate, which could arise by reductive elimination from intermediate **LIII**, formed by an oxidative cyclometallation. A conrotatory ring opening of the cyclobutene would explain formation of the rearranged diene.

Mechanistic studies based on ^{2}H- and ^{13}C-labeling experiments[195] revealed that products of type A and type B (*Scheme XLVI*) were formed depending on the substitution of the enyne. This suggested that two mechanistic pathways could be operating in the reaction with terminal acetylenes (*Scheme XLIX*). However, when R = CO_2Me, the reaction follows exclusively *path a*. Thus, the initial palladabicyclo[3.3.0]octene (**LIV**), formed by oxidative cyclometallation, was proposed to give the coordinated cyclobutene **LV** by a reductive elimination. A conrotatory ring opening of **LV** gives *type A* cyclopentene. Enynes with unsubstituted alkynes, or those bearing alkyl substituents, could suffer a ring contraction from **LV** to the stabilized cyclopropylcarbinyl palladacyclopentadienyl anion **LVI**. Cleavage of either bonds "a" or "b" would account for the formation of *type*

[194] (a) Trost. B. M.; Trost, M. K. *Tetrahedron Lett.* **1991**, *32*, 3647-3650. (b) Trost. B. M.; Trost, M. K. *J. Am. Chem. Soc.* **1991**, *113*, 1850-1852. (c) Trost, B. M.; Chang, V. K. *Synthesis* **1993**, 824-832.
[195] Trost, B. M.; Czeskis, B. A. *Tetrahedron Lett.* **1994**, *35*, 211-214.

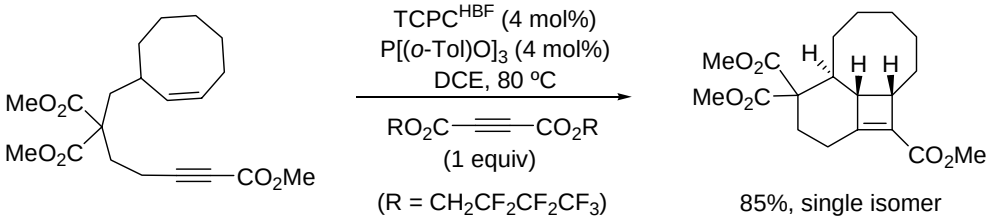
A and *type B* cycles, respectively. Alternatively, these enynes can follow the *path b*, in which **LIV** rearranges to the palladacyclopropylcarbene **LVII**, which after several steps gives rise to *type B* cyclopentene.



Scheme XLIX. *Postulated mechanism for skeletal rearrangement.*

The isolation of some cyclobutenes or isomerized cyclobutenes formed from the reaction of 1,6-,[194a,b] 1,7-,[150] and 1,8-enynes[150] with TCPC^{HBF} supports their participation in the Pd-catalyzed skeletal rearrangement of enynes (*Scheme L*). Increasing the tether length of the enyne and the presence of electron-withdrawing groups on the alkyne were crucial for the isolation of these cyclobutenes.

[150] Trost, B. M.; Yanai, M.; Hoogsteen, K. *J. Am. Chem. Soc.* **1993**, *115*, 5294-5295.
[194] (a) Trost. B. M.; Trost, M. K. *Tetrahedron Lett.* **1991**, *32*, 3647-3650. (b) Trost. B. M.; Trost, M. K. *J. Am. Chem. Soc.* **1991**, *113*, 1850-1852.



Scheme L. *Synthesys of fused cyclobutenes.*

As shown before, this Pd-catalyzed reaction is highly selective only in the case of enynes having an electron-withdrawing group on the alkyne and a *cis* alkene. However, many other electrophilic metal complexes promote the skeletal rearrangement of enynes. Thus, Trost and coworkers described the skeletal rearrangement of enynes catalyzed by $[Pd(PPh_3)_2(OAc)_2]$ and $[Pt(PPh_3)_2(OAc)_2]$.[194c] Additionally, $[RuCl_2(CO)_3]_2$, and other Ru complexes, $[RhCl(CO)_2]_2$, $[ReCl(CO)_5]$, $AuCl_3$,[153a] and $[IrCl(CO)_3]_n$[165] promote the skeletal rearrangement of enynes when the reaction is carried out under CO atmosphere. $PtCl_2$,[153,196] $PtCl_4$,[153e] and other cationic Pt complexes,[197] as well as the Lewis acid $GaCl_3$,[153,198] are also effective catalysts for this reaction. Furthermore, research group of Echavarren has extensively reported that Au(I) complexes as very active catalysts for the skeletal rearrangement.[154] The reaction with these catalysts is more general, and 1,6-enynes having terminal or internal alkynes and di- or trisubstituted alkenes are rearranged to vinylcyclopentenes in good yields.

Additional advantages of these new catalytic systems are, for instance, the exclusively *E* geometry of the vinyl moiety, regardless the geometry of the starting enyne, and even

[153] (a) Chatani, N.; Morimoto, T.; Muto, T.; Murai, S. *J. Am. Chem. Soc.* **1994**, *116*, 6049-6050. (b) Chatani, N.; Furukawa. N.; Sakurai, H.; Murai, S. *Organometallics* **1996**, *15*, 901-903. (c) Chatani, N.; Kataoka. K.; Murai, S.; Furukawa, N.; Seki, Y. *J. Am. Chem. Soc.* **1998**, *120*, 9104-9105. (d) Chatani, N.; Inoue, H.; Kotsuma, T.; Murai, S. *J. Am. Chem. Soc.* **2002**, *124*, 10294-10295. (e) Ho-Oh, C.; Youn-Bang, S.; Yun-Rhim, C. *Bull. Korean Chem. Soc.* **2003**, *24*, 887-888.

[154] (a) Nieto-Oberhuber, C.; Muñoz, M. P.; Buñuel, E.; Nevado, C.; Cárdenas, D. J.; Echavarren, A. M. *Angew. Chem., Int. Ed.* **2004**, *43*, 2402-2406. (b) Nieto-Oberhuber, C.; Muñoz, M. P.; López, S.; Jiménez-Nuñez, E.; Nevado, C.; Herrero-Gómez, E.; Raducan, M.; Echavarren, A. M. *Chem. Eur. J.* **2006**, *12*, 1677-1693. (c) Cabello, N.; Rodríguez, C.; Echavarren, A. M. *Synlett* **2007**, 1753-1758. (d) Jiménez-Núñez, E.; Claverie, C. K.; Bour, C; Cárdenas, D. J.; Echavarren, A. M. *Angew. Chem., Int. Ed.* **2008**, *47*, 7892-7895. (e) Bartolom,e, C.; Ramiro, Z.; Pérez-Galán, P.; Bour, C.; Raducan, M.; Echavarren, A. M.; Espinet, P. *Inorg. Chem.* **2008**, *47*, 11391-11397.

[165] Chatani, N.; Inoue, H.; Morimoto, T.; Muto, T.; Murai, S. *J. Org. Chem.* **2001**, *66*, 4433-4436.

[194] (c) Trost, B. M.; Chang, V. K. *Synthesis* **1993**, 824-832.

[196] (a) Fürstner, A.; Szillat, H.; Gabor, B.; Mynott, R. *J. Am. Chem. Soc.* **1998**, *120*, 8305-8314. (b) Fürstner, A.; Szillat, H.; Stelzer, F. *J. Am. Chem. Soc.* **2000**, *122*, 6785-6786.

[197] Oi, S.; Tsukamoto, I.; Miyano, S.; Inoue, Y. *Organometallics* **2001**, *20*, 3074-3079.

[198] $InCl_3$ has been also described as catalyst for these reactions: Miyanohana, Y.; Chatani, N. *Org. Lett.* **2006**, *8*, 2155-2158.

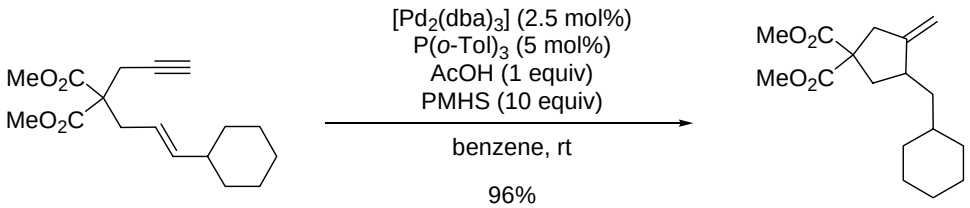
1,7-enynes can be effectively transformed in 1-alkenylcyclohexenes in contrast to that found by Trost and coworkers.[193]

2.3 Enyne Tandem Cyclization/Functionalization Reactions

The success of Pd-catalyzed, and other transition metal-catalyzed, cycloisomerizations in the synthesis of a large variety of carbo- and heterocycles with a high level of selectivity under mild conditions has prompted the development of tandem reactions, with the goal to further extend the level of functionalization of the products and provide a very attractive way to reach complex target molecules by using highly atom-economical transformations. Thereby, several tandem reactions such as reductive and oxidative cyclizations, nucleophilic additions, metalation reactions, and polycyclizations have been developed with success.

2.3.1 Reductive Cyclizations

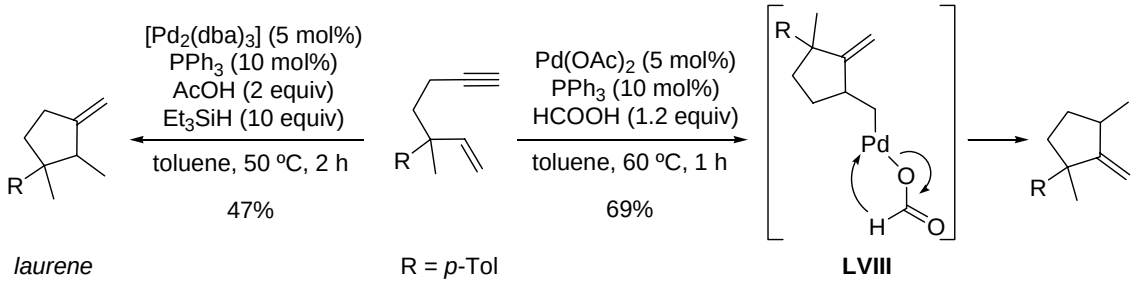
In the course of earlier investigations on the cycloisomerization of enynes, Trost and Rise[199] reported the reaction of an enyne in the presence of polymethylhydroxisiloxane (PMHS) giving the cycloreductive product as a single isomer, that is, the catalyst system is perfectly compatible with the presence of extra double bond (*Scheme LI*). On the basis of cross-labeling experiments, an alkyl palladium complex of type **XLVI** (*Scheme XXXIII*) was invoked as the key intermediate, wich is susceptible to undergo reduction in the presence of Si-H groups as hydrogen donors.



Scheme LI. *Si-H-mediated reductive cyclization.*

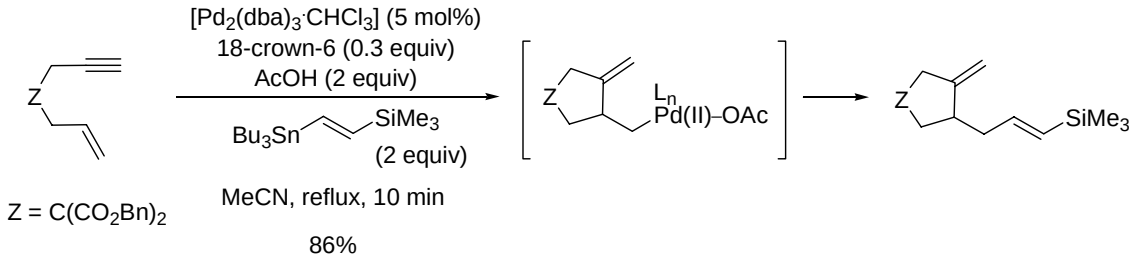
[193] Trost, B. M.; Tanoury, G. J. *J. Am. Chem. Soc.* **1988**, *110*, 1636-1638.
[199] Trost, B. M.; Rise, F. *J. Am. Chem. Soc.* **1987**, *109*, 3161-3163.

Alternatively to this method, Oh and Jung[200] described system based on the use of a stoichiometric amount of formic acid , which plays a dual role in the reaction pathway incorporating both hydrogen atoms in the cyclized reduced product. First of all, in accordance with the mechanism depicted in *Scheme XXXIII* to form the active Pd–H species, and secondly, cleavage of the formate ion from intermediate **LVIII** gives again a Pd–H species that undergoes reductive elimination (*Scheme LII*).



Scheme LII. *Formic acid and Si-H-mediated reductive cyclizations.*

These methologies have been applied to the total synthesys of natural products such as ceratopicanol[201] and laurene (*Scheme LII*).[202] Other reductive methods such as the employ of H_2 can be found in the literature.[203]



Scheme LIII. *Reductive cyclization via Stille coupling.*

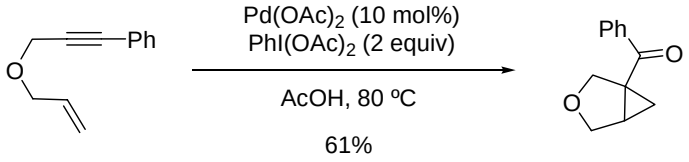
Similar strategies have been developed for alkylative cyclization sequences of enynes. For instance, in the presence of alkenyltin reagents, a cross-coupling step related to the

[200] (a) Oh, C. H.; Jung, H. H. *Tetrahedron Lett.* **1999**, *40*, 1535-1538. (b) Oh, C. H.; Jung, H. H.; Kim, J. S.; Cho, S. W. *Angew. Chem., Int. Ed.* **2000**, *39*, 752-755.
[201] Oh, C. H.; Rhim, C. Y.; Kim, M.; Park, D. I.; Gupta, A. K. *Synlett* **2005**, 2694-2696.
[202] Oh, C. H.; Han, J. W.; Kim, J. S.; Um, S. Y.; Jung, H. H.; Jang, W. H.; Won, H. S. *Tetrahedron Lett.* **2000**, *41*, 8365-8369.
[203] Jang, H.-Y.; Krische, M. *J. Am. Chem. Soc.* **2004**, *126*, 7875-7880.

Stille reaction takes place with the alkyl palladium complex of type **XLVI** (*Scheme XXXIII*) and leads to allyl-substituted carbo- and heterocycles (*Scheme LIII*).[204]

2.3.2 Oxidative Cyclizations

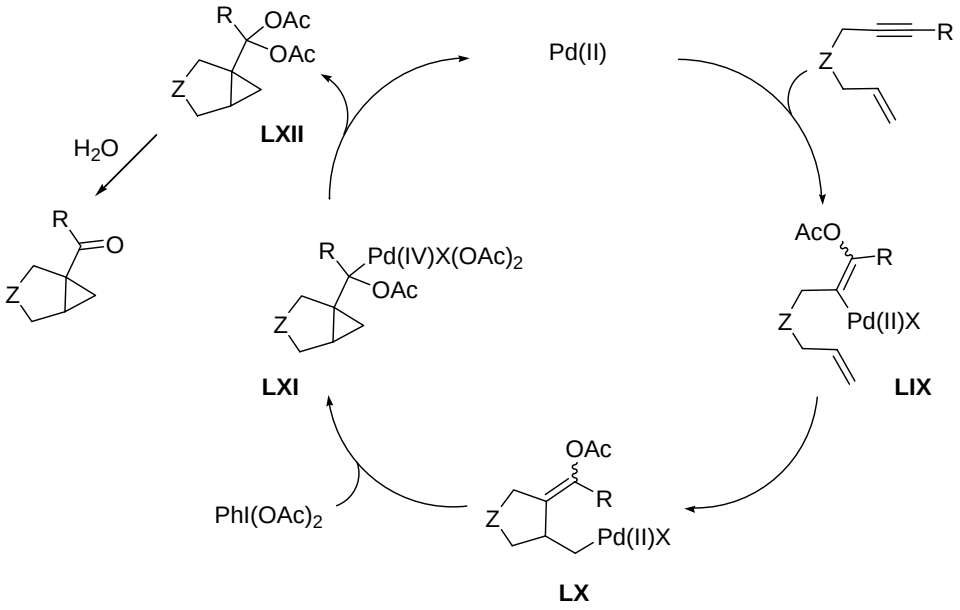
In the last years, the first examples of oxidative cyclization of 1,6-enynes have been developed. Thus, research groups of Tse[205] and Sandford[206] have described, independantly, the formation of cyclopropylketones through this oxidative method (*Scheme LIV*).



Scheme LIV. *Synthesis of cyclopropylketones.*

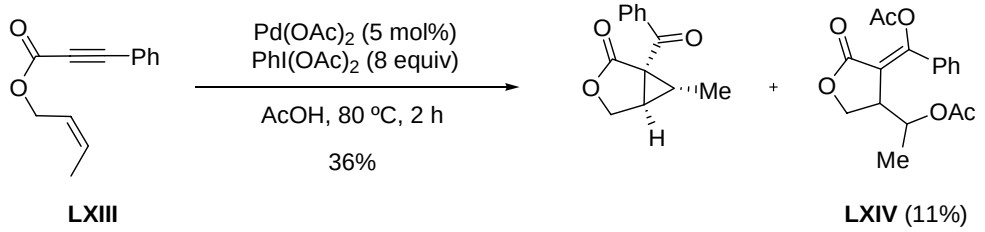
In a typical experiment, an enyne is treated with the oxidating agent (diacetoxyiodo)benzene in the presence of $Pd(OAc)_2$ in acetic acid at 80 ºC to give a cyclopropylketone in modest yield. The reaction scope of the transformation is large, as a wide range of alkyl and aryl substituents as well as ynone and ynamide functionalities are tolerated. One of the most important features of the reaction is that both research groups postulate a mechanism involving Pd(IV) intermediates (*Scheme LV*). In a first step, acetoxypalladation of the triple bond proceeds in a trans fashion to give the vinylpalladium intermediate **LIX**. Subsequent alkene insertion provides the alkyl palladium species **LX**. Oxidation of the palladium center and cyclopropanation by insertion into the enol ester function produce the alkyl Pd(IV) intermediate **LXI**. Reductive elimination releases the active Pd(II) species and **LXII**, which gives the cyclopropylketone upon hydrolysis.

[204] Yamada, H.; Aoyagi, S.; Kibayashi, C. *Tetrahedron Lett.* **1997**, *38*, 3027-3030.
[205] Tong, X.; Beller, M.; Tse, M. K. *J. Am. Chem. Soc.* **2007**, *129*, 4906-4907.
[206] Weibes, L. L.; Lyons, T. W.; Cychosz, K. A.; Sanford, M. S. *J. Am. Chem. Soc.* **2007**, *129*, 5836-5837.



Scheme LV. *Postulated mechanism for oxidative cyclization.*

The existence of the alkyl palladium species **LX** is backed up by the isolation of a diacylated lactone of type **LXIV** as a by-product upon oxidative cyclization of enyne **LXIII** (*Scheme LVI)*).



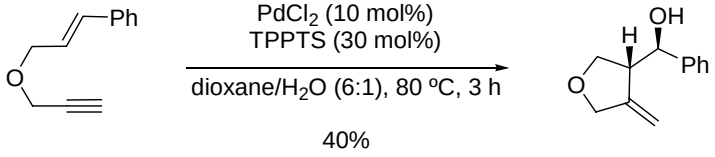
Scheme LVI. *Evidence of the proposal mechanism.*

2.3.3 Nucleophilic Additions

In the course of studies directed towards the application of aqueous organic conditions to the cycloisomerization of 1,6-enynes, Genêt and coworkers discovered the first carbohydroxypalladation reaction.[207] The reaction was catalyzed by $PdCl_2$ and the water-soluble phosphine TPPTS (*m*-sulfonated triphenyl phosphine) in an homogeneous mixture of dioxanne and water, to give five member rings with an hydroxyl group in a

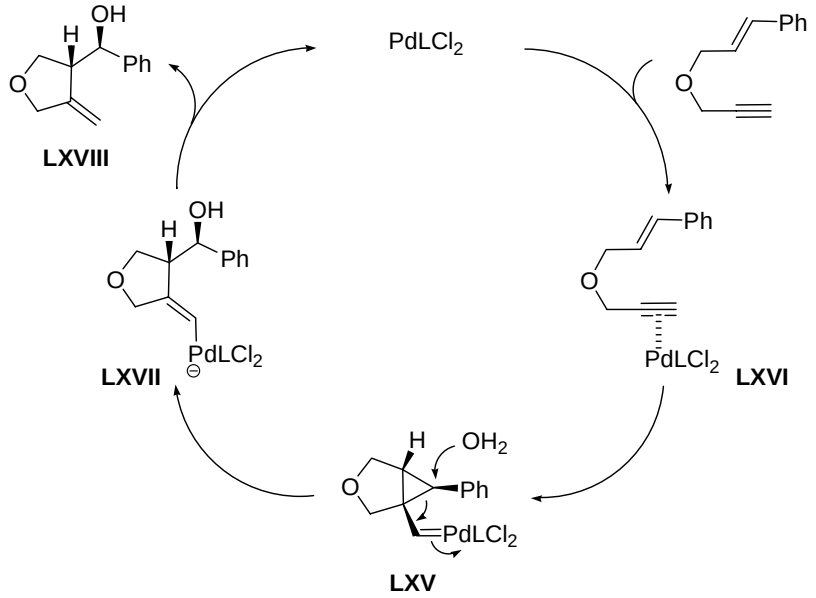
[207] (a) Galland, J.-C.; Savignac, M.; Genêt, J.-P. *Tetrahedron Lett.* **1997**, *38*, 8695-8698. (b) Galland, J.-C.; Savignac, M.; Genêt, J.-P. *Tetrahedron* **2001**, *57*, 5137-5148. (c) Charruault, L.; Michelet, V.; Genêt, J.-P. *Tetrahedron Lett.* **2002**, *43*, 4757-4760.

diastereoespecific manner (*Scheme LVII*). Other oxygen nucleophiles such as MeOH were also introduced diastereoselectively.



Scheme LVII. *First carbohydroxipalladation reported.*

From deuterium labeling experiments, and in accord with more recent mechanistic investigations on Pt- and Au-related transformations, the reaction is believed to proceed via the formation of a cyclopropylcarbene complex **LXV**.[208] The key step of this cyclization is the coordination of the metal to the alkyne affording the corresponding (η^2-alkyne)metal complex **LXVI**. This coordination favors the nucleophilic attack of the alkene to form the metal cyclopropyl carbene **LXV** that can suffer the nucleophilic attack of the solvent, giving rise to **LXVII**. Finally, subsequent demetalation gives ether **LXVIII** (*Scheme LVIII*).

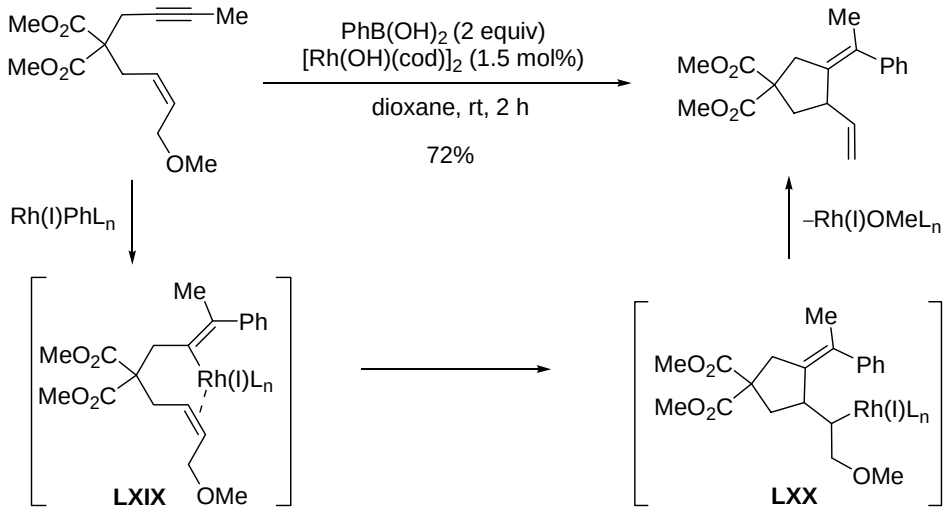


Scheme LVIII. *Hydroxicyclization mechanistic pathway.*

[208] Nevado, C.; Charrualult, L.; Michelet, V.; Nieto-Oberhuber, C.; Muñoz. M. P.; Méndez, M.; Rager, M.-N.; Genêt, J.-P.; Echavarren, A. M. *Eur. J. Org. Chem.* **2003**, 706-713.

As mentioned above, other catalyst such as Pt(II)[149d-f] and Au(I),[154] or even Hg(II)[209] are able to carry out the reaction by a similar pathway.

On the other hand, organometallic reagents have also been used as nucleophilic partners in cycloisomerization reactions.[210] For instance, Murakami and coworkers developed the Rh-catalyzed addition of arylboronic acids to 1,6-enynes (*Scheme LIX*).[211] The reaction is initiated by regioselective addition of a phenyl-rhodium(I) species, generated *in situ* by the transmetallation of Rh(I) with phenylboronic acid, onto the alkyne, giving the alkenyl–Rh(I) intermediate **LXIX**. Intramolecular carborhodation to the pendent allylic double bond then occurs in a 5-*exo* mode, leading to the formation of the alkyl–Rh(I) intermediate **LXX**. Finally, *β*-elimination of methoxy group affords the final diene with generation of a catalytically active Rh(I) methoxide.



Scheme LIX. *Rh-catalyzed addition of arylboronic acids.*

[149] (d) Méndez, M.; Muñoz, M. P.; Echavarren, A. M. *J. Am. Chem. Soc.* **2000**, *122*, 11549-11550. (e) Méndez, M.; Muñoz, M. P.; Nevado, C.; Cárdenas, D. J.; Echavarren, A. M. *J. Am. Chem. Soc.* **2001**, *123*, 10511-10520. (f) Muñoz, M. P.; Méndez, M.; Nevado, C.; Cárdenas, D. J.; Echavarren, A. M. *Synthesis* **2003**, 2898-2902.

[154] (a) Nieto-Oberhuber, C.; Muñoz, M. P.; Buñuel, E.; Nevado, C.; Cárdenas, D. J.; Echavarren, A. M. *Angew. Chem., Int. Ed.* **2004**, *43*, 2402-2406. (b) Nieto-Oberhuber, C.; Muñoz, M. P.; López, S.; Jiménez-Nuñez, E.; Nevado, C.; Herrero-Gómez, E.; Raducan, M.; Echavarren, A. M. *Chem. Eur. J.* **2006**, *12*, 1677-1693. (c) Cabello, N.; Rodríguez, C.; Echavarren, A. M. *Synlett* **2007**, 1753-1758. (d) Jiménez-Núñez, E.; Claverie, C. K.; Bour, C; Cárdenas, D. J.; Echavarren, A. M. *Angew. Chem., Int. Ed.* **2008**, *47*, 7892-7895. (e) Bartolom,e, C.; Ramiro, Z.; Pérez-Galán, P.; Bour, C.; Raducan, M.; Echavarren, A. M.; Espinet, P. *Inorg. Chem.* **2008**, *47*, 11391-11397.

[209] Nishizawa, M.; Yadav, V. K.; Skwarcynski, M.; Takao, H.; Imagawa, H.; Sugihara, T. *Org. Lett.* **2003**, *5*, 1609-1611.

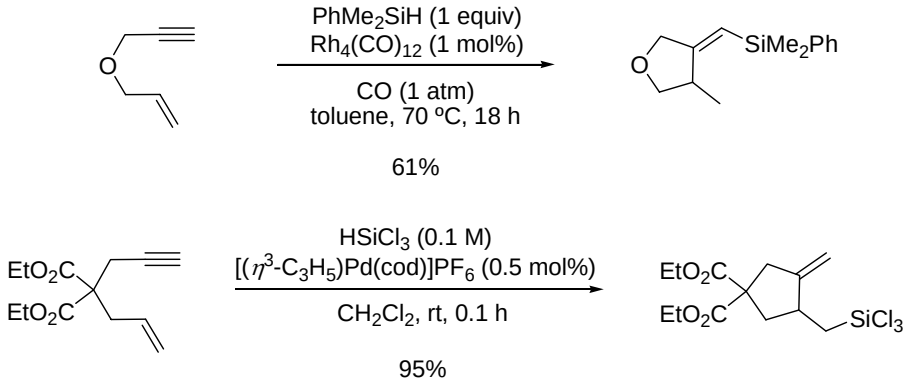
[210] Hanzawa, Y.; Yabe, M.; Oka, Y.; Taguchi, T. *Org. Lett.* **2002**, *4*, 4061-4064.

[211] Miura, T.; Shimada, M.; Murakami, M. *J. Am. Chem. Soc.* **2005**, *127*, 1094-1095.

2.3.4 Metalation Reactions

In view of their versatility as partners in cross-coupling reactions and the large number of accessible synthetic transformations, attention has been focused on methodologies that allow the synthesis of complex organometallic reagents. The addition of metal–hydrogen or metal–metal reagents to carbon–carbon multiple bonds represents a well-established approach towards this end.[212] Some examples of the application of this concept to the field of cycloisomerization of 1,n-enynes have been described in the literature using Rh and Pd as main catalysts.

Regarding to the addition of metal–hydrogen reagents to enynes, tandem cyclization/hydrometalation reactions have been reported with Si, Sn, and B. Hydrosilylation of 1,6-enynes was firstly reported by Ojima and coworkers using Rh as catalyst under CO atmosphere (*Scheme LX*).[213]



Scheme LX. *Hydrosilylation of enynes.*

This reaction afforded the alkenylsilyl-cyclized products in moderate to good yields with a large scope. In the last years the process has been improved as a result of the employ of other catalysts[214] such as cationic Rh complexes,[215] which carry out the reaction with high levels of enantioselectivity. Complementary, Yamamoto and coworkers reported later that Pd cationic complexes are able to catalyze the

[212] Beletskaya, I.; Moberg, C. *Chem. Rev.* **2006**, *106*, 2320-2354.

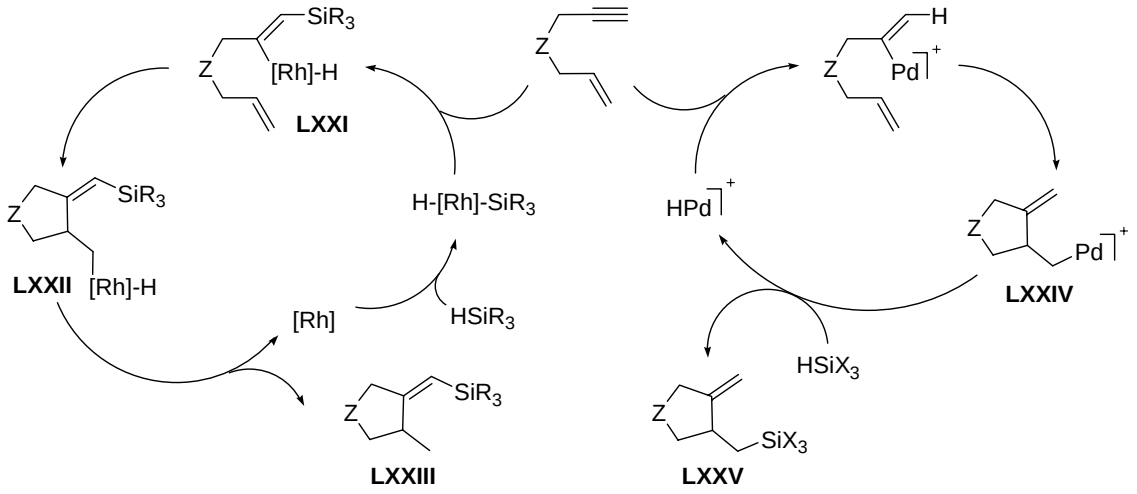
[213] (a) Ojima, I.; Donovan, R. J.; Shay, W. R. *J. Am. Chem. Soc.* **1992**, *114*, 6580-6582. (b) Ojima, I.; Vu, A. T.; Lee, S.-L.; McCullagh, J. V.; Moralee, A. C.; Fujiwara, M.; Hoang, T. H. *J. Am. Chem. Soc.* **2002**, *124*, 9164-9174.

[214] For Rh N-heterocyclic carbene complex: (a) Park, K. H.; Kim, S. Y.; Son, S. U.; Chung, Y. K. *Eur. J. Org. Chem.* **2003**, 4341-4345. For organoyttrium complex: (b) Retsch, G. H.; Molander, G. A. *J. Am. Chem. Soc.* **1997,** *119,* 8817-8825.

[215] (a) Chakrapani, H.; Liu, C.; Widenhoefer, R. A. *Org. Lett.* **2003**, *5*, 157-159. (b) Fan, B.-M.; Xie, J.-H.; Li, S.; Wang, L.-X.; Zhou, Q.-L. *Angew. Chem., Int. Ed.* **2007**, *46*, 1275 –1277.

hydrosilylation, however, in this case alkylsilyl-cyclized products were obtained (*Scheme LX*).[216]

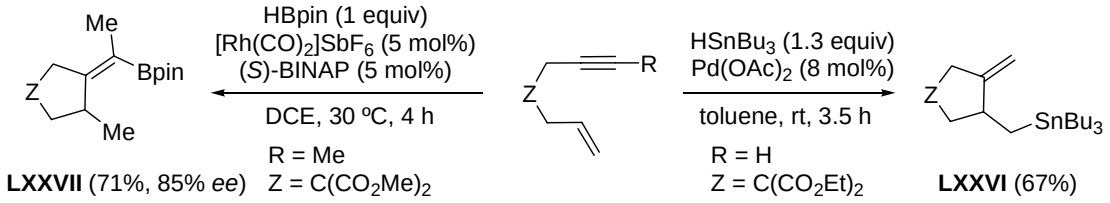
The different behaviour between two catalytic processes relies on the mechanistic pathways (*Scheme LXI*). Rh-catalyzed process starts with the oxidatively formation of H-Rh-Si species, next step is the insertion of the alkyne into the Rh-Si bond to give alkenyl–Rh–H intermediate (**LXXI**), which undergoes carbometalation of the alkene moiety affording the alkyl–Rh–H intermediate **LXXII**, and finally, reductive elimination to obtain **LXXIII**. On the other hand, cationic Pd complex follows a similar pathway that shown in *Scheme XXXIII*, in which, the key alkyl-Pd intermediate **LXXIV** undergoes a possible σ-metathesis with the corresponding hydrosilane to afford **LXXV**.



Scheme LXI. *Rh- and Pd-catalyzed hydrosilylation pathways.*

Furthermore, hydrostannylative cyclization of enynes has been reported by Lautens and coworkers using $Pd(OAc)_2$ as catalyst forming alkylstannyl-cyclized products (**LXXVI**, *Scheme LXII*).[217] In this case, Pd(II) reduces to Pd(0) by Bu_3SnH, which then oxidatively inserts into the Sn-H bond of other molecule of hydride. Hydropalladation of the acetylenic moiety then occurs, followed by carbopalladation of the double bond and final reductive elimination.

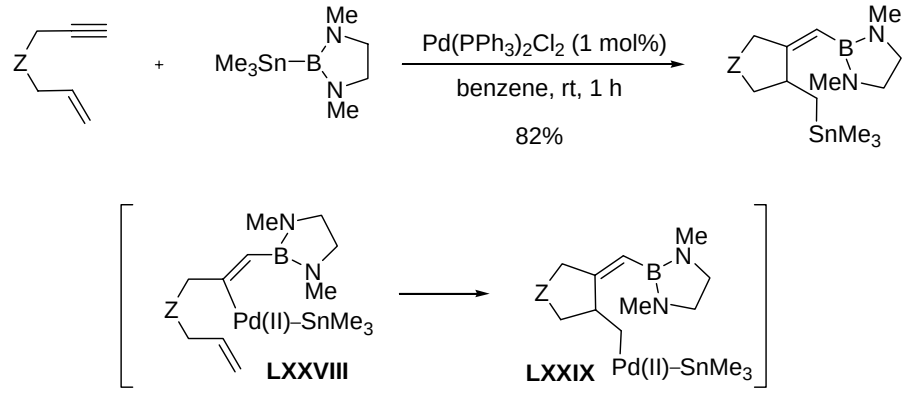
[216] (a) Wakayanagi, S.; Shimamoto, T.; Chimori, M.; Yamamoto, K. *Chem. Lett.* **2005**, *2*, 160-161. (b) Shimamoto, T.; Chimori, M.; Sogawa, H.; Yamamoto, K. *J. Am. Chem. Soc.* **2005,** *127,* 16410-16411.
[217] Lautens, M.; Mancuso, J. *Org. Lett.* **2000**, *2*, 671-673.



Scheme LXII. *Hydrostannylation and hydroborylation of enynes.*

Hydroborylative cyclization also has been described in a cationic Rh complex-catalyzed process (*Scheme LXII*).[218] This reaction reported by Widenhoefer and coworkers follows a similar pathway as mentioned above for hydrosilylation with Rh catalyst and affords alkenylboryl-cyclized products (**LXXVII**) in good yields.

Finally, the addition of metal–metal reagents to cyclization procceses of enynes has been described with some metal combinations. Thus, borylsilylation,[219] borylstannylation,[75] and silylstannylation[220] procceses among others take place under Pd-catalyzed conditions affording bimetallic-cyclized compounds (*Scheme LXIII*) that can be, in many cases, selectively functionalizated. The general mechanistic pathway involves oxidative addition of bimetallic species to Pd(0), followed by insertion of the alkyne into the more reactive Pd–M bond giving the vinylpalladium complex (**LXXVIII**). Subsequent insertion of the alkene unit and reductive elimination from **LXXIX** leads to the final product and regenerates the catallytically active species.

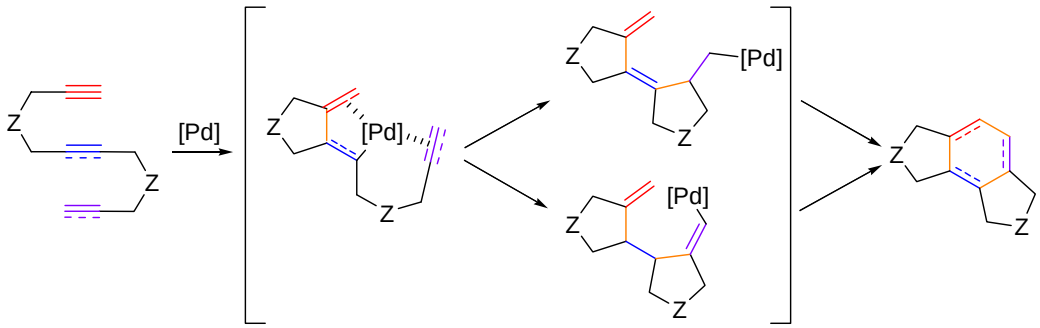


Scheme LXIII. *Pd-catalyzed borylstannilation of enynes.*

[75] Onozawa, S.; Hatanaka, Y.; Choi, N.; Tanaka, M. *Organometallics* **1997**, 1*6*, 5389-5391.
[218] Kinder, R., E.; Widenhoefer, R. A. *Org. Lett.* **2006**, *8*, 1967-1969.
[219] Onozawa, S.Y.; Hatanaka, Y.; Tanaka, M. *Chem. Commun.*, **1997**,1229-1230.
[220] (a) Mori, M.; Hirose, T.; Wakamatsu, H.; Imakuni, N.; Sato, Y. *Organometallics* **2001**, *20*, 1907-1909. (b) Sato, Y.; Imakuni, N.; Hirose, T.; Wakamatsu, H.; Mori, M. *J. Organomet. Chem.* **2003**, *687*, 392-402.

2.3.5 Polycyclization Sequences

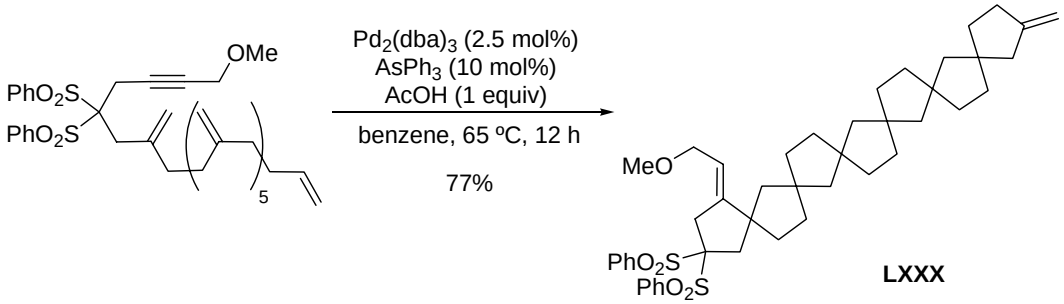
One of the most attractive potentials of the possibility of trapping an alkenyl- or alkyl-Pd intermediate is the intramolecular insertion into an electrophilic part of the molecule such a double or a triple bond. By this way a large variety of highly strained polyciclic structures can be achieved through this extension of the original Alder-ene reaction. Thereby, Trost and coworkers[158e,221] have extensively reported the Pd-catalyzed polycyclization reaction of enediynes leading to bicyclic or tricyclic compounds in a single operation and also the mechanistic pathways have been studied there in, following the same features than the simple enynes such as vinylmetal or cyclometallation pathways (*Scheme LXIV*).



Scheme LXIV. *Pd-catalyzed polycyclization of enediynes.*

This appealing methodology has been extended to triynes and other poliinsaturated compounds as a result of the great number of possible combinations. Thus, an spectacular example is the synthesis of polyspirane **LXXX** in one step with a good yield (*Scheme LXV*).[222]

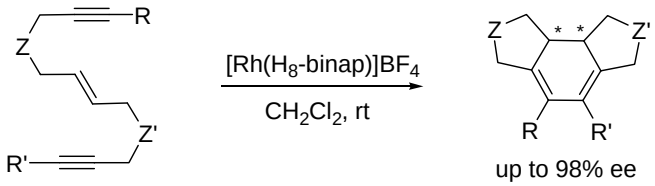
[158] (e) Trost, B. M.; Tanoury, G. J.; Lautens, M.; Chan, C.; MacPherson, D. T. *J. Am. Chem. Soc.* **1994**, *116*, 4255-4267.
[221] (a) Trost, B. M.; Lee, D. C. *J. Am. Chem. Soc.* **1988,** *110,* 7255-7258. (b) Trost, B. M.; Lee, D. C. *J. Org. Chem.* **1989,** *54,* 2274-2275. (c) Trost, B. M.; Shi, Y. *J. Am. Chem. Soc.* **1993,** *115,* 12491-12509.
[222] (a) Trost, B. M.; Shi, Y. *J. Am. Chem. Soc.* **1991,** *113,* 701-703. (b) Trost, B. M.; Shi, Y. *J. Am. Chem. Soc.* **1993,** *115,* 9421-9438.



Scheme LXV. *Pd-catalyzed synthesis of polyspiranes.*

In addition, many research groups have developed this kind of Pd-catalyzed cycloaddition reaction by modification of the tethers, that is, introduction of acetylene groups, heteroatom-bridged chains, substitution on the alkene moiety, etc.[223]

Furthermore, as equal with enynes, depending on the catalyst, several mechanistic pathways can be accessed with the concomitant influence at the final products. For instance, Shibata and coworkers reported Rh-catalyzed intramolecular [2+2+2] cycloaddition of enediynes giving tricycles with a high level of enantioselectivity (*Scheme LXVI*).[224]

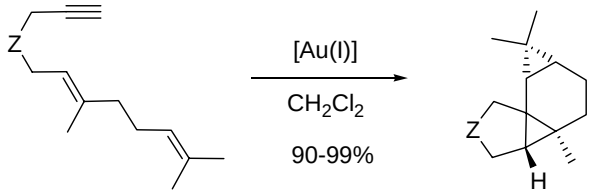


Scheme LXVI. *Rh-catalyzed enantioselective polycyclization of enediynes.*

On the other hand, when the mechanistic pathway outcomes through carbene-metal species, another type of cycles can be obtained such as cyclopropanes. Following this approach, metals such as Pd,[225] Ru,[226] Au[227] or Pt[228] are able to catalyze the synthesis of a great variety of fused polycycled natural products (*Scheme LXVII*).

[223] (a) Negishi, E.-I.; Harring, L. S.; Owczarczyk, Z.; Mohamud, M. M.; Ay, M. *Tetrahedron Lett.* **1992**, *33*, 3253-3256. (b) Oh, C. H.; Rhim, C. Y.; Kang, J. H.; Kim, A.; Park, B. S.; Seo, Y. *Tetrahedron Lett.* **1996**, *37*, 8875-8878. (c) Yamamoto, Y.; Nagata, A.; Arikawa, Y.; Tatsumi, K.; Itoh, K. *Organometallics* **2000**, *19*, 2403-2405. (d) Yamamoto, Y.; Nagata, A.; Nagata, H.; Ando, Y.; Arikawa, Y.; Tatsumi, K.; Itoh, K. *Chem. Eur. J.* **2003**, *9*, 2469-2483. (e) Yamamoto, Y.; Kuwabara, S.; Ando, Y.; Nagata, H.; Nishiyama, H.; Itoh, K. *J. Org. Chem.* **2004,** *69,* 6697-6705. (f) Tokan, W. M.; Schweizer, S.; Thies, C.; Meyer, F. E.; Parsons, P. J.; de Meijere, A. *Helv. Chim. Acta* **2009**, *92*, 1729-1740.

[224] Shibata, T.; Kurokawa, H.; Kanda, K. *J. Org. Chem.* **2007,** *72,* 6521-6525.



Scheme LXVII. *Polycylization via metal-carbene pathway.*

Finally, taking advantage of the possibility of trapping the metal-intermediates, tandem cyclization/metalation processes have been also applied to the polycyclization sequences. By this way, Ojima and coworkers[213,229] extended their Rh-mediated hydrosilylation conditions to enediynes, and even developed carbonylative carbotricyclizations with these poliinsaturated substrates (*Scheme LXVIII*).

In this case the alkyl–Rh–H intermediate **LXXXI**, formed after the insertion of alkyne into the Si–Rh bond and the first cyclization, is effectively trapped by the other acetylene moiety to form the alkenyl–Rh–H intermediate **LXXXII**. Subsequent reductive elimination leads to the silyl-bicycle product (*Scheme LXVIII*). Although the trapping of the alkenyl-Rh species with the vinylsilane moiety to undergo the third carbocyclization is conceptually possible, this cyclization does not take place.

[213] (a) Ojima, I.; Donovan, R. J.; Shay, W. R. *J. Am. Chem. Soc.* **1992**, *114*, 6580-6582 (b) Ojima, I.; Vu, A. T.; Lee, S.-L.; McCullagh, J. V.; Moralee, A. C.; Fujiwara, M.; Hoang, T. H. *J. Am. Chem. Soc.* **2002**, *124*, 9164-9174.

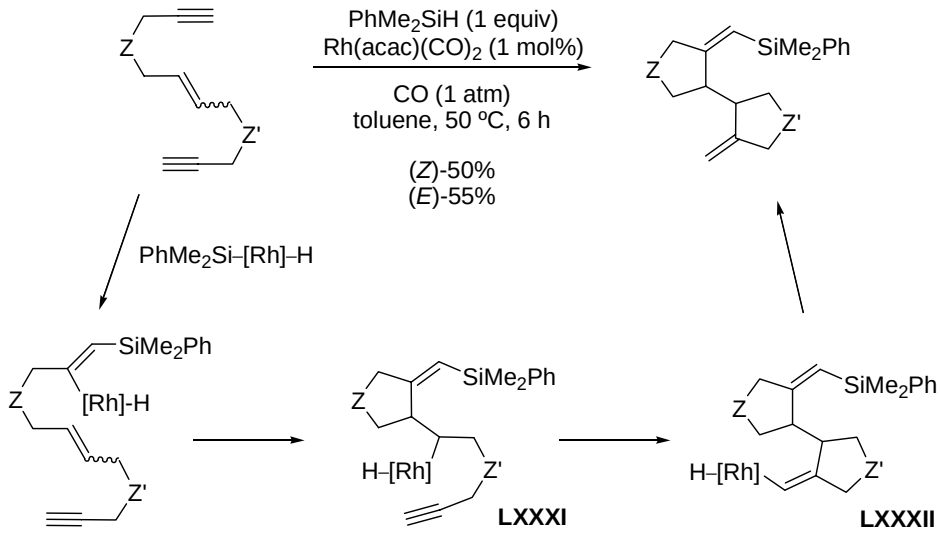
[225] (a) Trost, B. M.; Hahsmi, S. K. *Angew. Chem., Int. Ed.* **1993**, *32*, 1085-1087. (b) Trost, B. M.; Hahsmi, S. K. *J. Am. Chem Soc.* **1994**, *116*, 2183-2184. (c) Trost, B. M.; Hashmi, A. S. K.; Ball, R. G. *Adv. Synth. Catal.* **2001**, *343*, 490-494.

[226] Chatani, N.; Kataoka, K.; Murai, S. *J. Am. Chem. Soc.* **1999**, *120*, 9104-9105.

[227] Nieto-Oberhuber, C.; López, S.; Muñoz, M. P.; Jímenez-Nuñez, E.; Buñuel, E.; Cárdenas, D. J.; Echavarren, A. M. *Chem. Eur. J.* **2006**, *12*, 1694-1702.

[228] Mainetti, E.; Mouriès, V.; Fensterbank, L.; Malacria, M.; Marco-Contelles, J. *Angew. Chem. Int., Ed.* **2002**, *41*, 2132-2135.

[229] (a) Ojima I.; McCullagh J. V.; Shay, W. R. *J. Organomet. Chem.* **1996**, *521*, 421-423. (b) Ojima, I.; Lee, S-Y. *J. Am. Chem. Soc.* **2000,** *122,* 2385-2386. (c) Bennacer, B.; Fujiwara, M.; Lee, S-Y.; Ojima, I. *J. Am. Chem. Soc.* **2005,** *127,* 17756-17767.



Scheme LXVIII. *Tandem hydrosylilative polycylization.*

3. Transition Metal-Catalyzed Allenyne and Enallene Cyclization

Compared with alkynes and alkenes, allenes have been much less studied as a component for the catalytic formation of carbon–carbon multiple bonds. However, allenes have demostrated to be versatile intermediates for organic synthesis in recent years.[230,231]

When one of the insaturated moieties of an enyne is remplaced by an allene, two different substrates can be envisioned (*Figure VI*). Thus, if the alkene is changed, an allenyne is obtained (**LXXXIII**), whereas if is the alkyne, an enallene is achieved (**LXXXIV**).

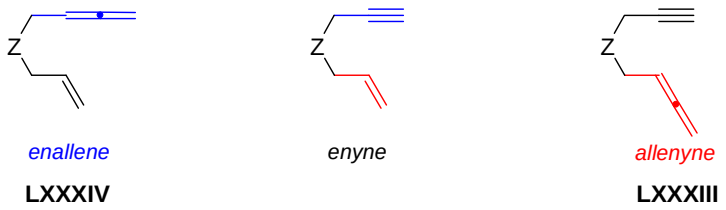


Figure VI. *Enallenes and allenynes.*

It is worthwhile to note that these changes, mainly the presence of the allene moiety, affect directly to the reactivity under transition metal-catalyzed conditions, and therefore, making possible the preparation of a large variety of new cyclized products.

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[230] For recent progress in the chemistry of allenes: (a) Hashmi, A. S. K. *Angew. Chem., Int. Ed.* **2000**, *39*, 3590-3593. (b) *Modern Allene Chemistry*; Krause, N.; Hashmi, A. S. K., Eds.; Wiley-VCH: Weinheim, Germany 2004; Vols. 1-2. (c) Hassan, H. H. A. M. *Curr. Org. Synth.* **2007**, *4*, 413-439.

[231] For metalation and bismetalation reactions of allenes. Hydroboration: (a) Ess, D. H.; Kister, J.; Chen, M.; Roush, W. R. *Org. Lett.* **2009**, *11*, 5538-5541. Hydrosilylation (b) Sudo, T.; Asao, N.; Gevorgyan, V.; Yamamoto, Y. *J. Org. Chem.* **1999,** *64,* 2494-2499. Hydrostannylation: (c) Lautens, M.; Ostrovsky, D.; Tao, B. *Tetrahedron Lett.* **1997**, *38*, 6343-6346. Diboration: (d) Ishiyama, T.; Kitano, T.; Miyaura, N. *Tetrahedron Lett.* **1998**, *39*, 2357-2360. (e) Yang F.-Y.; Cheng C.-H. *J. Am. Chem. Soc.* **2001**, *123*, 761-762. (f) Pelz, N. F.; Woodward, A. R.; Burks, H. E.; Sieber, J. D.; Morken, J. P. *J. Am. Chem. Soc.* **2004**, *126*, 16328-16329. (g) Pelz, N. F.; Morken, J. P. *Org. Lett.* **2006**, *8*, 4557-4559. (h) Sieber, J. D.; Morken, J. P. *J. Am. Chem. Soc.* **2006**, *128*, 74-75. (i) Burks, H. E.; Liu, S.; Morken, J. P. *J. Am. Chem. Soc.* **2007**, *129*, 8766-8773. Silylboration: (j) Suginome, M.; Ohmori, Y.; Ito, Y. *J. Organomet. Chem.* **2000**, *611*, 403-413. (k) Suginome, M.; Ohmura, T.; Miyake, Y.; Mitani, S.; Ito, Y.; Murakami, M. *J. Am. Chem. Soc.* **2003**, *125*, 11174-11175. (l) Chang, K.-J.; Rayabarapu, D. K.; Yang, F.-Y.; Cheng, C.-H. *J. Am. Chem. Soc.* **2005**, *127*, 126-131. (m) Ohmura, T.; Taniguchi, H.; Suginome, M. *J. Am. Chem. Soc.* **2006**, *128*, 13682-13683. Borylstannylation: (n) Onozawa, S.; Hatanaka, Y.; Tanaka, M. *Chem. Commun.* **1999**, 1863-1864. Disilylation: (o) Watanabe, H.; Saito, M.; Sutou, N.; Nagai, Y. *Chem. Commun.* **1981**, 617-618. (p) Watanabe, H.; Saito, M.; Sutou, N.; Kishimoto, K.; Inose, J.; Nagai, Y. *J. Organomet. Chem.* **1982**, *225*, 343-356. Distannylation: (q) Killing, H.; Mitchell, T. *Organometallics* **1984**, *3*, 1318-1320. (r) Mitchell, T. N.; Kwetkat, K.; Rutschow, D.; Schneider, U. *Tetrahedron* **1989**, *45*, 969-978. (s) Kwetkat, K.; Riches, B. H.; Rossett, J.-M.; Brecknell, D. J.; Byriel, K.; Kennard, C. H. L.; Young, D. J.; Schneider, U.; Mitchell, T. N.; Kitching, W. *Chem. Commun.* **1996**, 773-774. (t) Wesquet, A. O.; Kazmaier, U. *Angew. Chem., Int. Ed.* **2008**, *47*, 3050-3053. Silylstannylation: (u) Mitchell, T. N.; Killing, H.; Dicke, R.; Wickenkamp, R. *Chem. Commun.* **1985**, 354-355.

Herein, Pd-catalyzed processes in the chemistry of allenynes and enallenes will be comment predominantly.

3.1 Transition Metal-Catalyzed Allenyne Cyclization

Although transition metal-catalyzed cycloisomerization and carbocyclization processes have been less studied for allenynes with respect to enynes, transition metal catalyst such as Ti, Ru, Rh, Pd, Mo, Pt, and Au have been reported in the literature leading these reactions.[232,233] Besides, thermal cycloadditions of allenynes have also been described.[234]

As mentioned before, an allenyne is a substrate which is constituted by one alkyne and one allene. Differently to the homologous enynes, the presence of an allene moiety instead of the alkene changes the behaviour of a metal catalyst when the two species react. Whereas in the case of enynes, the mechanistic pathway always implied the coordination of the catalyst at least to the alkyne, now in allenynes, the two insaturated moieties compete for that coordination. In many cases, factors such as the presence in the molecule of electron-withdrawing groups or other directing groups, lead the coordination of the metal to the alkyne or to the allene moiety.

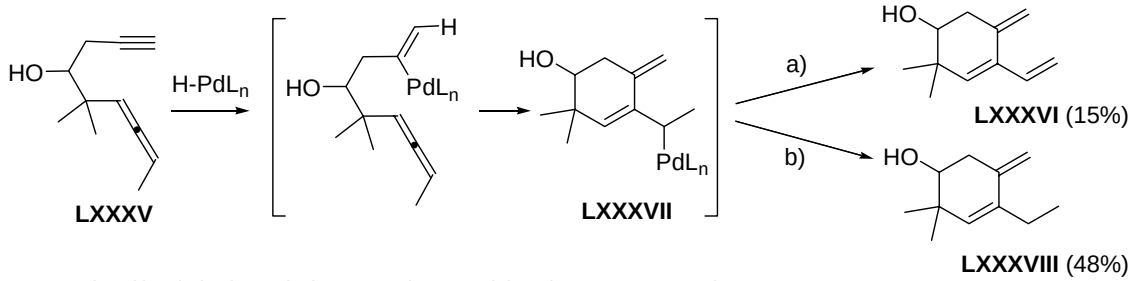
For instance, Oh and coworkers described these two different mechanistic pathways for Pd-catalyzed cyclizations.[232e,f] Thus, when allenyne **LXXXV** is subjected under Pd(0)/carboxilic acid conditions, six-membered triene **LXXXVI** was obtained.[232e] This

[232] Selected recent references: Ti: (a) Urabe, H.; Takeda, T.; Hideura, D.; Sato, F. *J. Am. Chem. Soc.* **1997**, *119*, 11295-11305. Ru: (b) Saito, N.; Tanaka, Y.; Sato, Y. *Organometallics* **2009**, *28*, 669-671. Rh: (c) Brummond, K. M.; Chen, H.; Sill, P.; You, L. *J. Am. Chem. Soc*. **2002**, *124*, 15186-15187. (d) Mukai, C.; Inagaki, F.; Yoshida, T.; Kitagaki, S. *Tetrahedron Lett.* **2004**, *45*, 4117-4121. Pd: (e) Oh, C. H.; Jung, S. H.; Rhim, C. Y. *Tetrahedron Lett*. **2001**, *42*, 8669-8671. (f) Oh, C. H.; Jung, S. H.; Park, D. I.; Choi, J. H. *Tetrahedron Lett*. **2004**, *45*, 2499-2502. Mo: (g) Shen, Q.; Hammond, G. B. *J. Am. Chem. Soc*. **2002**, *124*, 6534-6535. Pt: (h) Cadran, N.; Cariou, K.; Herve, G.; Aubert, C.; Fensterbank, L.; Malacria, M.; Marco-Contelles, J. *J. Am. Chem. Soc.* **2004**, *126*, 3408-3409. (i) Zriba, R.; Gandon, V.; Aubert, C.; Fensterbank, L.; Malacria, M. *Chem. Eur. J.* **2008**, *14*, 1482-1491. Au: (j) Lemière, G.; Gandon, V.; Agenet, N.; Goddard, J.-P.; de Kozak, A.; Aubert, C.; Fensterbank, L.; Malacria, M. *Angew. Chem., Int. Ed.* **2006**, *45*, 7596-7599. (k) Cheong, P. H.-Y.; Morganelli, P.; Luzung, M. R.; Houk, K. N.; Toste, F. D. *J. Am. Chem. Soc*. **2008**, *130*, 4517-4526.

[233] Alternative mechanisms for allenyne cycloisomerization: For Co, (a) Llerena, D.; Aubert, C.; Malacria, M. *Tetrahedron Lett.* **1996**, *37*, 7027-7030. For Ga, (b) Lee, S. I.; Sim, S. H.; Kim, S. M.; Kim, K.; Chung, Y. K. *J. Org. Chem.* **2006**, *71*, 7120-7123. For Hg, (c) Sim, S. H.; Lee, S. I.; Seo, J.; Chung, Y. K. *J. Org. Chem.* **2007**, *72*, 9818-9821. For Mo-catalyzed allenyne metathesis, (d) Murakami, M.; Kadowaki, S.; Matsuda, T. *Org. Lett.* **2005**, *7*, 3953-3956.

[234] Thermal reactions of allenynes: (a) Ohno, H.; Mizutani, T.; Kadoh, Y.; Miyamura, K.; Tanaka, T. *Angew. Chem., Int. Ed.* **2005**, *44*, 5113-5115. (b) Oh, C. H.; Gupta, A. K.; Park, D. I.; Kim, N. *Chem. Commun.* **2005**, 5670-5672. (c) Mukai, C.; Hara, Y.; Miyashita, Y.; Inagaki, F. *J. Org. Chem.* **2007**, *72*, 4454-4461. (d) Buisine, O.; Gandon, V.; Fensterbank, L.; Aubert, C.; Malacria, M. *Synlett* **2008**, 751-754. (e) Ovaska, T. V.; Kyne, R. E. *Tetrahedron Lett.* **2008**, *49*, 376-378.

product can be explained by hydropalladation of the alkyne followed by the formation of an alkyl-Pd intermediate **LXXXVII**, which undergoes *β*-hydrogen elimination (*Scheme LXIX*). In addition, that intermediate allows to carry out other tandem reactions such as reductive cyclization (**LXXXVIII**) mediated by Et_3SiH.



a) $Pd(PPh_3)_4$ (3 mol%), AcOH (1.2 equiv), toluene, 90 ºC, 3 h

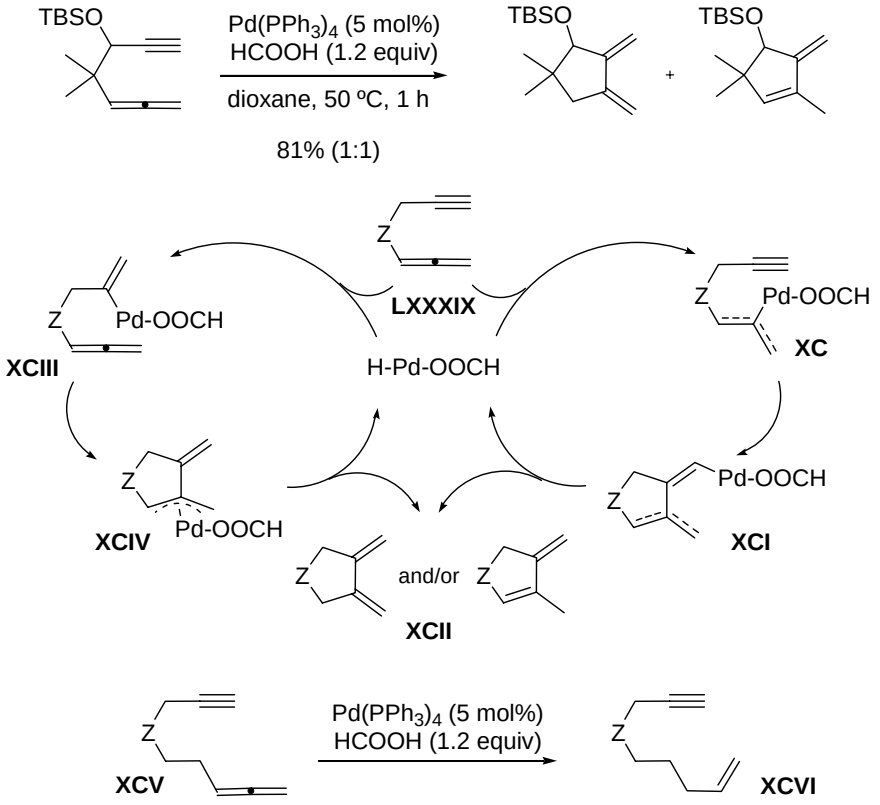
b) $Pd_2(dba)_3$ (3 mol%), P(*o*-Tol)$_3$ (3 mol%), Et_3SiH (3 equiv), AcOH (1.2 equiv), benzene, 50 ºC, 2 h

Scheme LXIX. *Proposed pathway via hydropalladation of the alkyne.*

On the other hand, the same research group reported another cycloreduction,[232f] in which, the H–Pd species reacts with one of the double bonds of the allene moiety (**LXXXIX**) to form the vinyl-Pd intermediates **XC**, where always Pd is linked to the central carbon of the original allene. Subsequent carbopalladation with the acetylene functionality to form the alkenyl-Pd intermediates **XCI** and finally, reductive cleavage of the pendant formate ligand affords five-membered diene products **XCII** (*Scheme LXX*).

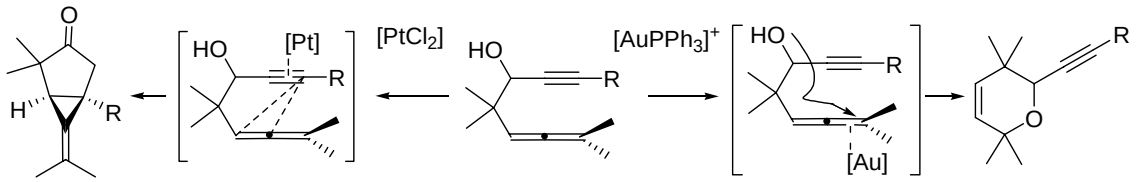
Although the products (**XCII**) can also be explained through the reaction of the H–Pd species with the alkyne to form the alkenyl-Pd intermediate **XCIII**, then carbopalladation of the allene moiety to form *π*-allyl-Pd intermediate **XCIV**, and finally reductive cleavage, the authors proposed the first mentioned pathway due to the result of the reaction of allenyne **XCV**, where only the allene suffers hydropalladation (**XCVI**) (*Scheme LXX*).

[232] (e) Oh, C. H.; Jung, S. H.; Rhim, C. Y. *Tetrahedron Lett*. **2001**, *42*, 8669-8671. (f) Oh, C. H.; Jung, S. H.; Park, D. I.; Choi, J. H. *Tetrahedron Lett*. **2004**, *45*, 2499-2502.



Scheme LXX. *Hydropalladation of the alkyne versus hydropalladation of the allene.*

Following with this interesting matter, Fensterbank and Malacria reported how metal catalysts such as Pt and Au can react differently with the same hydroxylated allenyne substrate.[232i] Thereby, Pt coordinates to the alkyne, whereas Au coordinates to the allene giving rise to absolutely different compounds (*Scheme LXXI*).

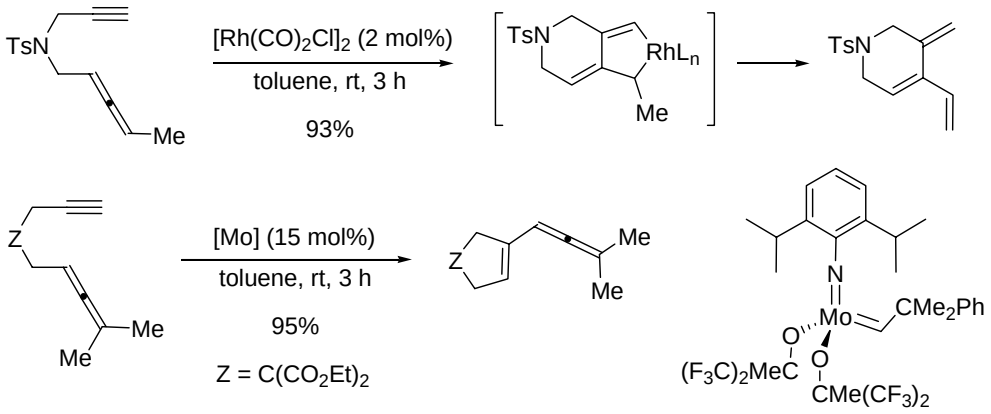


Scheme LXXI. *Different coordination depending upon the metal catalyst.*

Furthermore, other mechanistic pathways such as formation of metallacycle intermediates are possible with Ru,[232b] Rh[232c] or Pt[232h] as catalysts (*Scheme LXXII*).

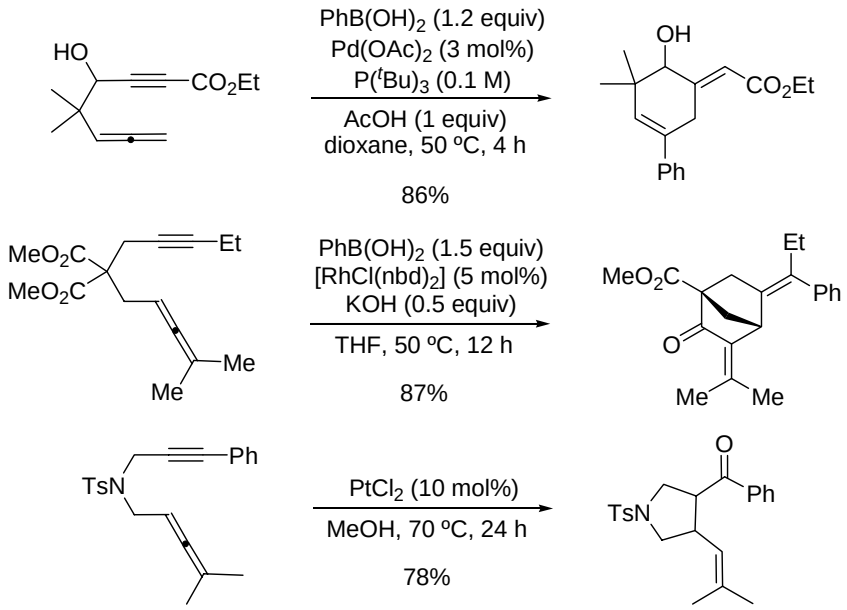
[232] Ru: (b) Saito, N.; Tanaka, Y.; Sato, Y. *Organometallics* **2009**, *28*, 669-671. Rh: (c) Brummond, K. M.; Chen, H.; Sill, P.; You, L. *J. Am. Chem. Soc*. **2002**, *124*, 15186-15187. Pt: (h) Cadran, N.; Cariou, K.; Herve, G.; Aubert, C.; Fensterbank, L.; Malacria, M.; Marco-Contelles, J. *J. Am. Chem. Soc.* **2004**, *126*, 3408-3409. (i) Zriba, R.; Gandon, V.; Aubert, C.; Fensterbank, L.; Malacria, M. *Chem. Eur. J.* **2008**, *14*, 1482-1491.

Even more, metathesis pathways have been described in the literature with Mo catalysts (*Scheme LXXII*).[233d]



Scheme LXXII. *Allenyne cycloisomerization via metallacycle or via metathesis pathways.*

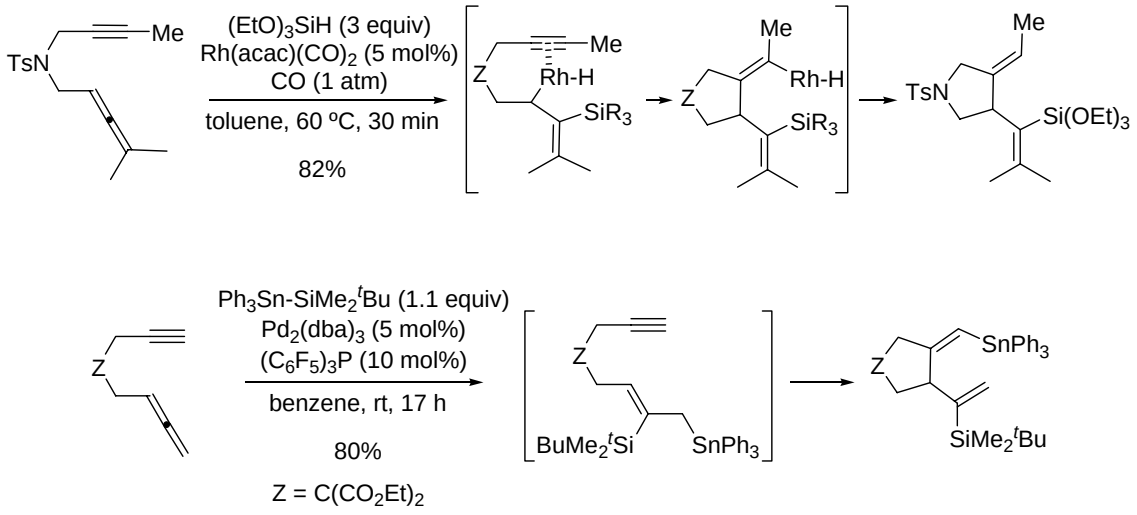
Regarding to the possible additional functionalization of the forming cycles by a tandem pathway, some processes have been described. Once again, research group of Oh reported the addition of organoboronic acids under Pd-catalysis following with their study of this addition on alkynes[137a] and allenes (*Scheme LXXIII*).[235]



Scheme LXXIII. *Addition of arylboronic acids and hydrative cyclization.*

[233] (d) Murakami, M.; Kadowaki, S.; Matsuda, T. *Org. Lett.* **2005**, *7*, 3953-3956.
[235] For allenynes: (a) Gupta, A. K.; Rhim, C. Y.; Oh, C. H. *Tetrahedron Lett.* **2005**, *46*, 2247-2250. For allenes: (b) Oh, C. H.; Ahn, T. W.; Reddy, V. R. *Chem. Commun.* **2003**, 2622-2623.

Later, Murakami and coworkers reported an analogous reaction catalyzed by Rh with arylboronic acids.[236] The latter group also decribed hydrative cyclization of allenynes catalyzed by Pt,[237] and later, Liu and coworkers catalyzed by Au (*Scheme LXXIII*).[238] Undoubtedly, processes in which main group elements are introduced along the cyclization reaction are especially important, since they allow the preparation of compounds which can be further functionalized. As mentioned in the case of the functionalization of enynes, allenynes can also perform tandem metalation/cyclization reactions. Thus, Shibata and coworkers reported the first hydrosilylative carbocyclization of allenynes,[239] and RajanBabu and coworkers the first silylstannilation- and distannylation-cyclization (*Scheme LXXIV*).[240]



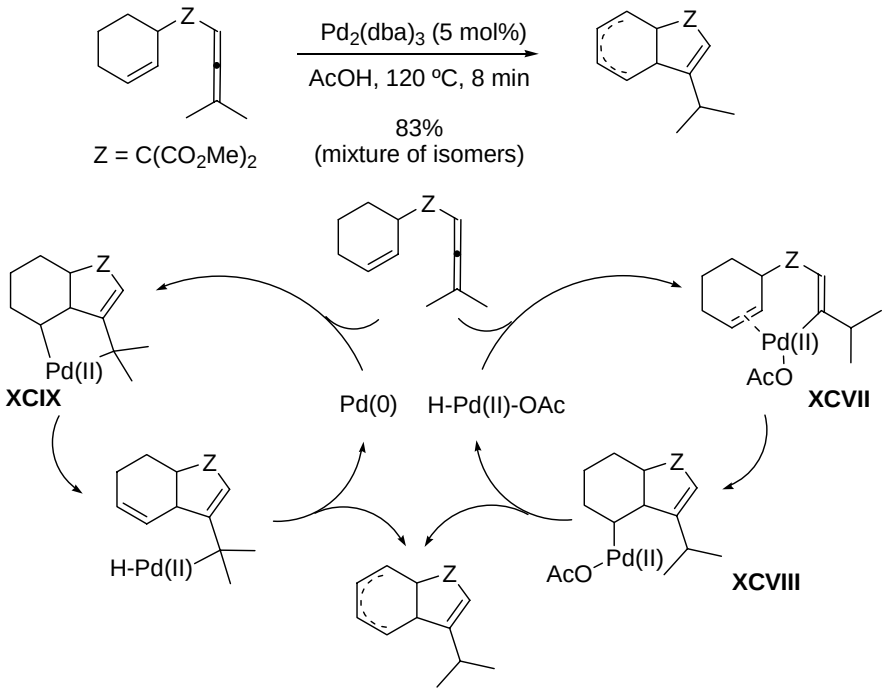
Scheme LXXIV. *Hydrosilylative and silylstannylation- cyclization of allenynes.*

[236] Miura, T.; Ueda, K.; Takahashi Y.; Murakami, M. *Chem. Commun*. **2008**, 5366-5368.
[237] Matsuda, M.; Kadowaki, S.; Murakami, M. *Helv. Chim. Acta* **2006**, *89*, 1672-1677.
[238] Yang, C.-Y.; Lin, G.-Y.; Liao, H.-Y.; Datta, S.; Liu, R.-S. *J. Org. Chem.* **2008,** *73,* 4907-4914.
[239] Shibata, T.; Kadowaki, S.; Takagi, K. *Organometallics* **2004**, *23*, 4116-4120.
[240] (a) Shin, S.; RajanBabu, T. V. *J. Am. Chem. Soc.* **2001**, *123*, 8416-8417. (b) Kumareswaran R.; Shin, S.; Gallou, I.; RajanBabu, T. V. *J. Org. Chem.* **2004**, *69*, 7157-7170.

3.2 Transition Metal-Catalyzed Enallene Cyclization

Chemistry of enallenes have been also developed in recent years. Thus, transition metal-catalyzed (Ru, Rh, Ni/Cr, Pd, Au) cycloisomerizations or carbocyclizations,[241] and thermal cycloadditions[242] can be found in the literature.

An enallene is a substrate which is formed by one alkene and one allene. In contrast to allenynes, the absence of the alkyne moiety facilitates the coordination of the metal, since the allene is more reactive than the alkene moiety. According to this fact, research group of Bäckvall proposed two possible mechanistic pathways for the Pd(0)-catalyzed cycloisomerization of enallenes (*Scheme LXXV*).[241f]



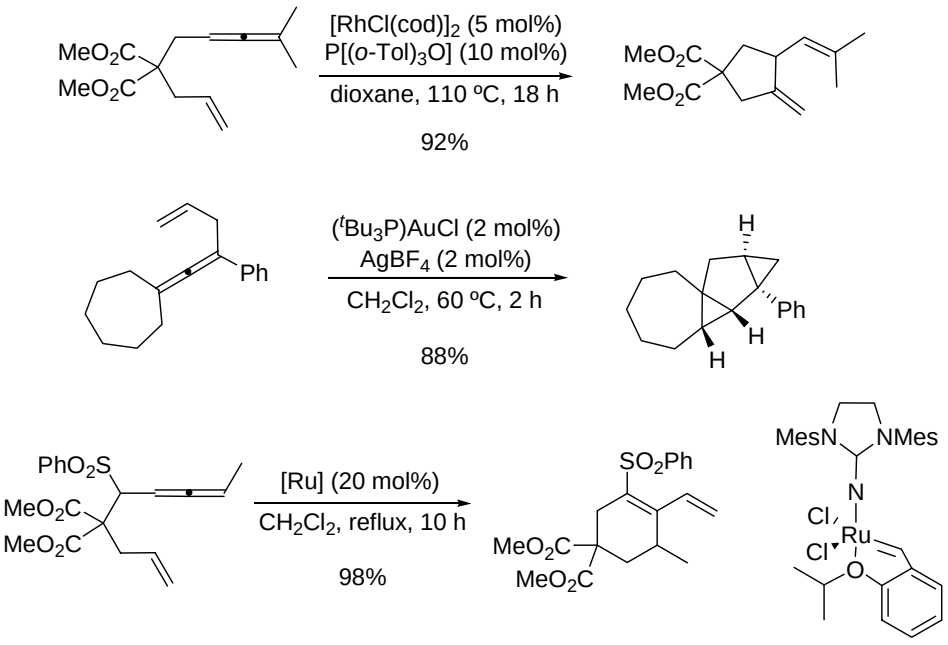
[241] Ru: (a) Mukai, C.; Itoh, R. *Tetrahedron Lett.* **2006**, *47*, 3971-3974. Rh: (b) Makino, T.; Itoh, K. *J. Org. Chem.* **2004**, *69*, 395-405. (c) Wender, P. A.; Glorius, F.; Husfeld, C. O.; Langkopf, E.; Love, J. A. *J. Am. Chem. Soc.* **1999**, *121*, 5348-5349. Ni/Cr: (d) Trost, B. M.; Tour, J. M. *J. Am. Chem. Soc.* **1988**, *110*, 5231-5233. Pd: (e) Trost, B. M.; Matsuda, K. *J. Am. Chem. Soc.* **1988**, *110*, 5233-5235. (f) Närhi, K.; Franzén, J.; Bäckvall J.-E. *Chem. Eur. J.* **2005**, *11*, 6937-6943. Au: (g) Lee, J. H.; Toste, F. D. *Angew. Chem., Int. Ed.* **2007**, *46*, 912-914. (h) Luzung M. R.; Mauleón P.; Toste, F. D. *J. Am. Chem. Soc.* **2007**, *129*, 12402-12403. (i) Tarselli, M. A.; Chianese, A. R.; Lee, S. J.; Gagné, M. R. *Angew. Chem., Int. Ed.* **2007**, *46*, 6670-6673. (j) Horino, Y.; Yamamoto, T.; Ueda, K.; Kuroda, S.; Toste, F. D. *J. Am. Chem. Soc.* **2009**, *131*, 2809-2811. (k) Marion, N.; Lemière, G.; Correa, A.; Costabile, C.; Ramón, R. S.; Moreau, X.; de Frémont, P.; Dahmane, R.; Hours, A.; Lesage, D.; Tabet, J.-C.; Goddard, J.-P.; Gandon, V.; Cavallo, L.; Fensterbank, L.; Malacria, M.; Nolan, S. P. *Chem. Eur. J.* **2009**, *15*, 3243-3260.

[242] Thermal reactions of enallenes: (a) Närhi, K.; Franzén, J.; Bäckvall J.-E. *J. Org. Chem.* **2006**, *71*, 2914-2917. (b) Ohno, H.; Mizutani, T.; Kadoh, Y.; Aso, A.; Miyamura, K.; Fujii, N.; Tanaka, T. *J. Org. Chem.* **2007**, *72*, 4378-4389.

Scheme LXXV. *Hydropalladation of the allene versus oxidative cycloaddition.*

First proposal pathway involves the oxidative addition of the solvent (AcOH) to Pd(0) giving rise to H–Pd(II) species. This H–Pd can then add to the terminal carbon atom of the allenic moiety resulting in a vinyl-Pd intermediate **XCVII**. An insertion of the double bond into the Pd–C bond would give **XCVIII**, which subsequently would undergo a *β*-hydride elimination to afford the product. The cycloisomerization can also be explained by an oxidative cycloaddition of the allene to Pd(0), forming the intermediate **XCIX**. Then, consecutive *β*-elimination and reductive elimination give rise to the final product. The formation of different isomers can be explained by consecutive *β* -eliminations and reinsertions by H–Pd species along the cyclohexene moiety.

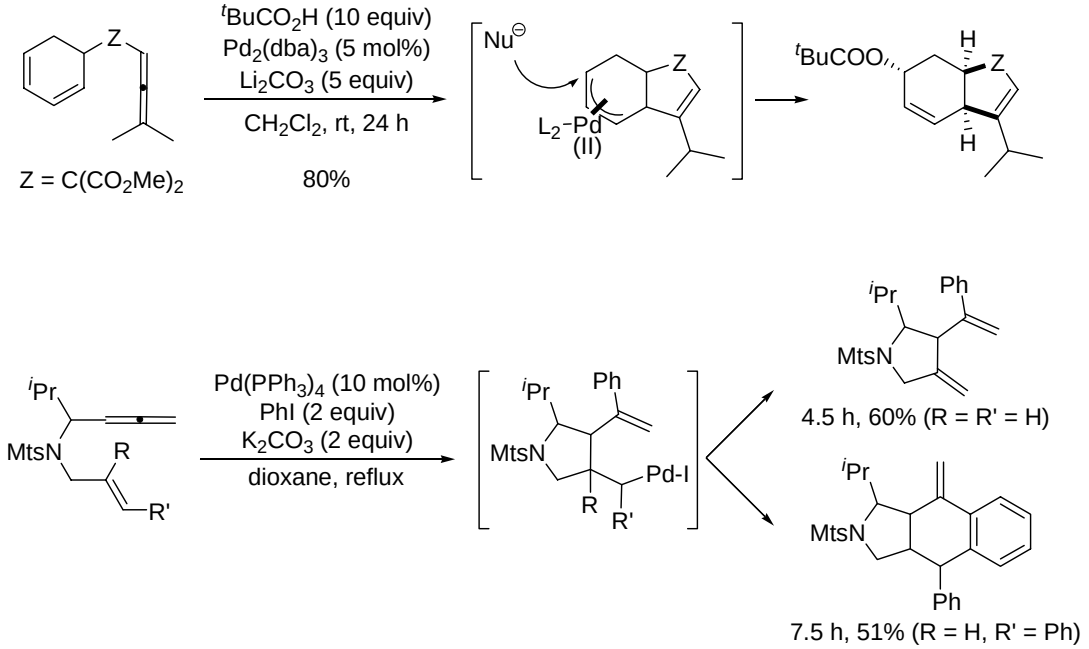
The use of other transition metal calalysts involve different mechanistic pathways (*Scheme LXXVI*). Thereby, Rh also undergo metallacycle intermediates,[241b] Au performs the reaction through metal-carbene and cationic intermediates,[241g-k] and even metathesis processes have been describe with Ru.[241a]



Scheme LXXVI. *Other metals catalyzed cycloisomerization of enallenes.*

[241] Ru: (a) Mukai, C.; Itoh, R. *Tetrahedron Lett.* **2006**, *47*, 3971-3974. Rh: (b) Makino, T.; Itoh, K. *J. Org. Chem.* **2004**, *69*, 395-405. Au: (c) Lee, J. H.; Toste, F. D. *Angew. Chem., Int. Ed.* **2007**, *46*, 912-914. (d) Luzung M. R.; Mauleón P.; Toste, F. D. *J. Am. Chem. Soc.* **2007**, *129*, 12402-12403. (e) Tarselli, M. A.; Chianese, A. R.; Lee, S. J.; Gagné, M. R. *Angew. Chem., Int. Ed.* **2007**, *46*, 6670-6673. (f) Horino, Y.; Yamamoto, T.; Ueda, K.; Kuroda, S.; Toste, F. D. *J. Am. Chem. Soc.* **2009**, *131*, 2809-2811. (g) Marion, N.; Lemière, G.; Correa, A.; Costabile, C.; Ramón, R. S.; Moreau, X.; de Frémont,

Finally, tandem cyclization/functionalization processes have also developed with enallenes (*Scheme LXXVII*).[230a,b] For instance, Bäckvall and coworkers described nucleophilic addition of water and others over allene-susbtituted conjugated dienes,[243] and Ohno and coworkers the direct construction of tricyclic heterocycles through aromatic C-H activation after addition of aryl halides.[244]



Scheme LXXVII. *Tandem cyclization/functionalization of enallenes.*

P.; Dahmane, R.; Hours, A.; Lesage, D.; Tabet, J.-C.; Goddard, J.-P.; Gandon, V.; Cavallo, L.; Fensterbank, L.; Malacria, M.; Nolan, S. P. *Chem. Eur. J.* **2009**, *15*, 3243-3260.

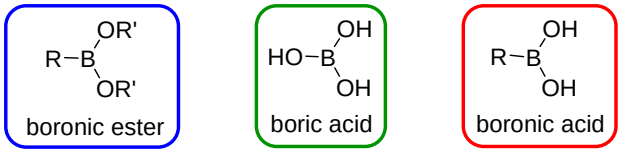
[230] (a) Hashmi, A. S. K. *Angew. Chem., Int. Ed.* **2000**, *39*, 3590-3593. (b) *Modern Allene Chemistry*; Krause, N.; Hashmi, A. S. K., Eds.; Wiley-VCH: Weinheim, Germany 2004; Vols. 1-2.

[243] (a) Löfstedt, J.; Franzén, J.; Bäckvall, J. E. *J. Org. Chem.* **2001**, *66*, 8015-8025. (b) Löfstedt, J.; Närhi, K.; Dorange, I.; Bäckvall, J. E. *J. Org. Chem.* **2003**, *68*, 7243-7248. (c) Dorange, I.; Löfstedt, J.; Närhi, K.; Franzén, J.; Bäckvall, J. E. *Chem. Eur. J.* **2003**, *9*, 3445-3449. (d) Franzén, J.; Bäckvall, J. E. *J. Am. Chem. Soc.* **2003**, *125*, 6056-6057. (e) Piera, J.; Persson, A.; Caldentey X.; Bäckvall, J.-E. *J. Am. Chem. Soc.* **2007**, *129*, 14120-14121.

[244] (a) Ohno, H.; Takeoka, Y.; Miyamura, K.; Kadoh, Y.; Tanaka, T. *Angew. Chem., Int. Ed*. **2003**, *42*, 2647-2650. (b) Ohno, H.; Takeoka, Y.; Miyamura, K.; Kadoh, Y.; Tanaka, T. *Org. Lett.* **2003**, *5*, 4763-4766. (c) Ohno, H.; Miyamura, K.; Mizutani, T.; Kadoh, Y.; Takeoka, Y.; Hamaguchi, H.; Tanaka, T. *Chem. Eur. J.* **2005**, *11*, 3728-3741.

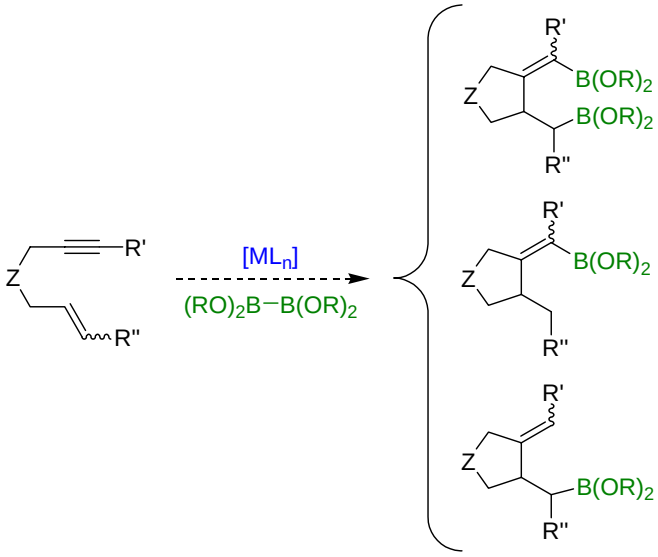
OBJECTIVES

As previously mentioned in the introduction, the development of innovative methologies for the synthesis of boron compounds is particularly useful for two main reasons: a) due to their importance as components on the preparation of more elaborated compounds by further functionalization (building blocks), and b) due to their prospective participation in the incoming "green" chemistry.



On the other hand, transition metal-catalyzed cyclization reactions from polyunsaturated acyclic compounds allow the construction of more complex organic species by tandem intramolecular trapping agents or even intermolecular partners. Moreover, these processes usually proceed with high levels of atom economy and selectivity.

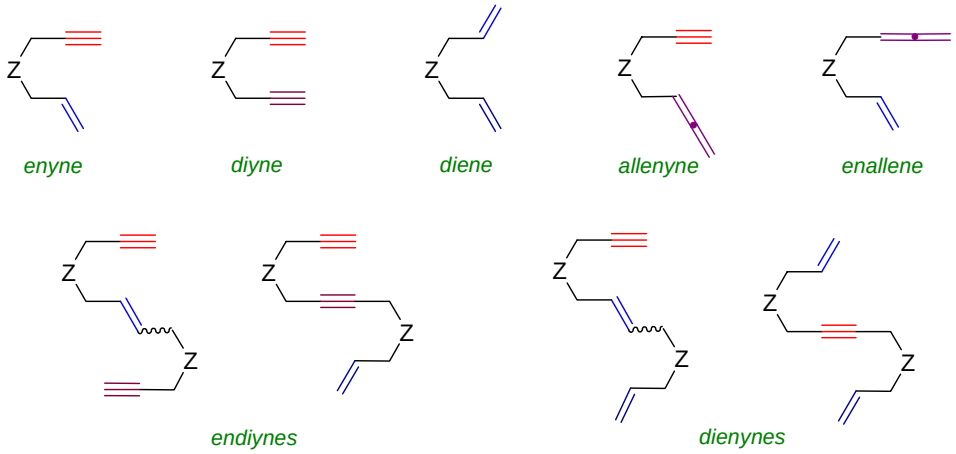
As a result of these two interesting fields to the synthesis of new organic compounds with potential applicability, the main objective of this research was the development of an original methodology in which new C–C and new C–B bonds were formed in a single operation.



In order to achieve that goal and following with analogous studies reported on the literature, Pd-catalyzed systems in the presence of bis(alcoxo)diboron compounds and polyunsaturated species, such as enynes, were the starting point of the research.

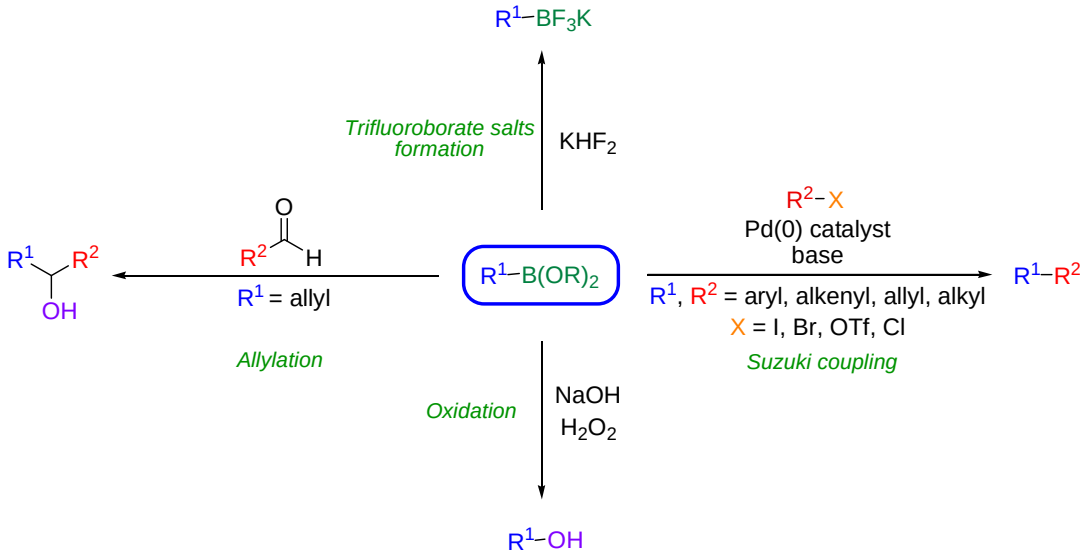
By this way, cyclic compounds with at least one new C–B bond could be formed. In addition, study was planned to clarify the mechanistic course of this process.

Secondly, the establishment of the scope of this new methodology by extending its applicability to other substrates, such as dienes, diynes or even allene-containing compounds (allenynes and enallenes), was considered. This study would allow the evaluation of several types of unsaturations under the optimized catalytic conditions.



Furthermore, this methodology could be apply to other substrates combining more than two unsaturated moieties (enediynes or dienynes). On these substrates more than one cyclization process could take place. Probably, the different disposition of the unsaturated moieties on the tether should lead to the formation of various polycyclic products depending upon the mechanistic pathways involved in each process.

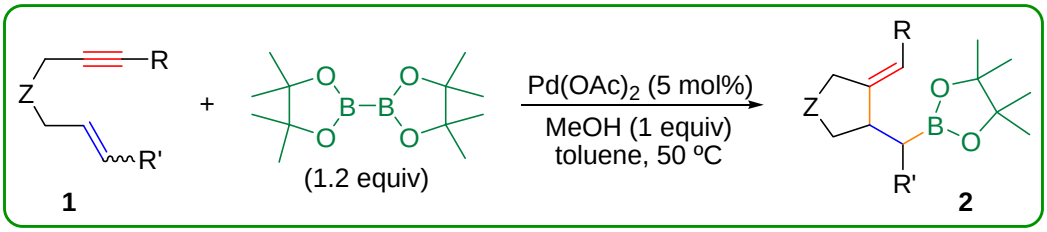
Finally, showing the synthetic versatility of the afforded boron compounds, studies of their further functionalization also seemed convenient. Depending on the hybridation of the carbon bonded to the boron (Csp^2–B, alkenylboron; or Csp^3–B, alkylboron) several known reactions could be carried out. Thus, oxidation, trifluoroborate salts formation, Suzuki coupling, and allylations were some of the most interesting examples for the transformation of the boron derivatives.


R1–BF3K
Trifluoroborate salts formation
KHF2
R2–X
Pd(0) catalyst
base
R1, R2 = aryl, alkenyl, allyl, alkyl
X = I, Br, OTf, Cl
Suzuki coupling
R1–R2
R1–B(OR)2
R1 = allyl
Allylation
Oxidation
NaOH
H2O2
R1–OH

RESULTS AND DISCUSSION

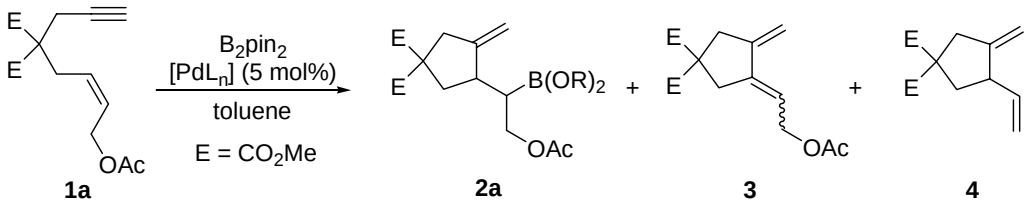
1. Pd-Catalyzed Borylative Cyclization of Enynes to Alkylboronates

The Pd-catalyzed reaction of 1,6-enynes (**1**) in the presence of bis(pinacolato)diboron has allow the synthesis of a large number of alkylboronates (**2**) by formation of two new bonds, one C–C and one C–B, and two new stereogenic centers in a single stereoselective operation,[245] as shown in the next scheme (*Scheme 1*):



Scheme 1. *Pd-catalyzed cyclization/borylation of enynes.*

Preliminary experiments showed that when enyne **1a** was reacted with bis(pinacolato)diboron in the presence of $Pd_2(dba)_3$·dba and PPh_3 in toluene, alkylboronate **2a** was obtained in low yield (*ca.* 20%), along with cycloisomerization derivative **3** and diene compound **4** in which the acetate group had been eliminated (*Scheme 2*).



Scheme 2. *Preliminary results of the reaction.*

The formation of **2a** implies a formal 1,7-hydroboration of the enyne with concomitant carbocyclization, affording a C–C and a C–B bond in a single operation (*Figure 1*). Incorporation of H probably took place from traces of water contained in the solvent.

[245] Marco-Martínez, J.; López-Carrillo, V.; Buñuel, E.; Simancas, R.; Cárdenas, D. J. *J. Am. Chem. Soc.* **2007**, *129*, 1874-1875.

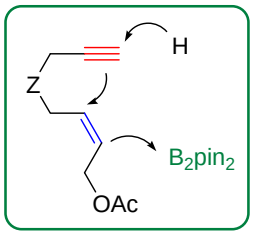


Figure 1. *Formal 1,7-hydroboration of an enyne.*

Optimization of the reaction conditions was performed by varying the solvent (toluene, dioxane, DMF), the precatalysts ($Pd_2(dba)_3$·dba, $PdCl_2$, $Pd(OAc)_2$, $Pd(PPh_3)_4$) and some additives (NaOAc, *n*-Bu_4NF or KF). It became apparent that the presence of phospines or additives favored the formation of **3** and **4**. The best results for the formation of **2a** (65% yield) were obtained by using $Pd(OAc)_2$ (5 mol%) as precatalyst in dry toluene in the presence of 0.5 equiv of pinacol as a proton source. The use of MeOH (1 equiv) instead of pinacol led to similar yields and was preferred since separation is easier in the absence of free pinacol, and transesterification of the boronic ester does not take place.

Compound **4** does not seem to be formed from **2a** since the latter did not decompose upon heating at 80 ºC for 24 h in dry toluene even in the presence of $Pd(dba)_2$ (5 mol%). In contrast, heating of **2a** in wet toluene gave diene **4**, probably by concerted elimination of the acetate and the boronic acid resulting from hydrolysis.

It is worthwhile to note that the presence of the key intermediate **A** may be probably invoked in the mechanistic pathway to afford the correspondent alkylboronate. Thus, that product (**2a**, R = H) could be achieved by reaction of the intermediate **A** with B_2pin_2 and followed by reductive elimination of the C–B bond (**II**, *Scheme 3*). It was reasoned that the presence of a coordinating group on the allylic position (OAc) and the additional presence of the exocyclic alkene would hamper *β*-hydride elimination in the putative intermediates (**A** and **B**).

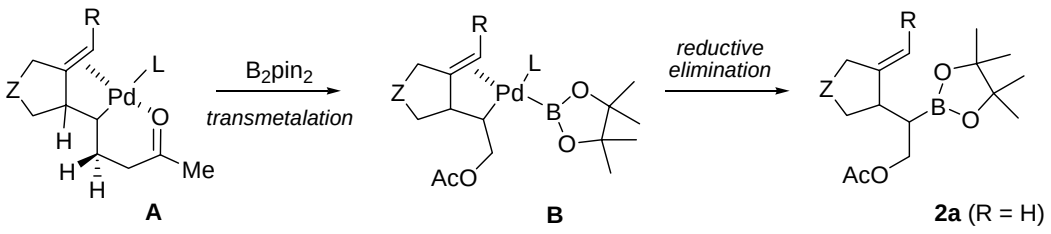
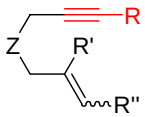


Figure 4. *Intramolecular coordinations avoiding β-hydride elimination.*

Next, in order to study the scope of the process, the reaction was extended to a large number of related substrates in which some modifications were included at the different moieties of the enyne. Those modifications were related with the following aspects of the initial substrate:

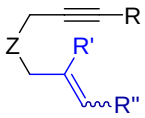
- The triple bond nature: terminal and internal alkynes.



R = H, Me, Ph, CO_2Me, $SiMe_3$

Figure 2. *Substitution on the triple bond.*

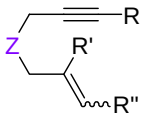
- The substitution on the alkene: monosubstituted, 1,1- and 1,2-disubstituted (*Z*/*E* geometry with coordinating groups: allylic esters and ethers, or non-coordinating groups: Me, Ph, and trisubstituted alkenes.



R' = H, Me, CH_2SO_2Ph
R'' = H, CH_2OAc, CH_2OBz, CH_2OMe, CH_2OBn, Me, Ph

Figure 3. *Substitution on the double bond.*

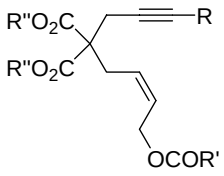
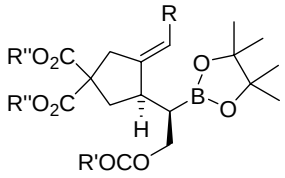
- The nature and substitution on the atom-bridge moiety: ether, amide, methylene or malonate (dimethyl, diethyl, bis(sulfonyl)methane) as tethers.



Z = O, NTs, CH_2, $C(CO_2Me)_2$, $C(CO_2Et)_2$, $C(SO_2Ph)_2$

Figure 4. *Substitution on the tether.*

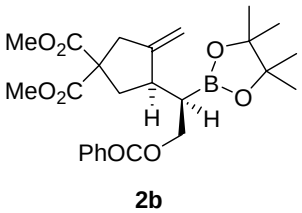
Regarding to the experiments performed with acetates and benzoates in the allylic position, **1a-e**, gave the corresponding alkylboronates (**2a-e**) in good to excellent yields (*Table 1*).

	substrate	time (h)	product	yield (%)
				
1	**1a**	2.5	**2a :** R = H, R' = Me, R'' = Me	59
2	**1b**	3	**2b :** R = H, R' = Ph, R'' = Me	76
3	**1c**	4	**2c :** R = Me, R' = Me, R'' = Et	95
4	**1d**	3.5	**2d :** R = Ph, R' = Me, R'' = Me	81
5	**1e**	50[a]	**2e :** R = $SiMe_3$, R' = Me, R'' = Et	79

[a] Additional $Pd(OAc)_2$ (5 mol%) and MeOH (1 equiv) were added after 25 h.

Table 1. *Alkylboronates from allylic ester derivatives.*

The obtention of single crystals of benzoate derivative **2b** suitable for X-ray diffraction allowed to assign the relative configuration for the new stereogenic centers (*Figure 5*).



2b

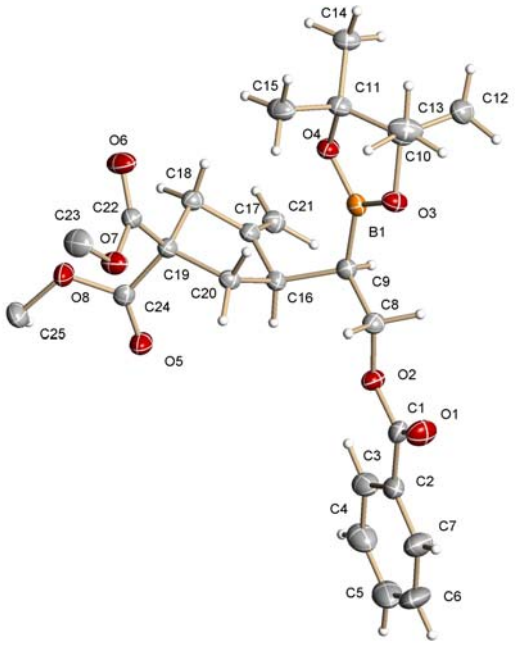
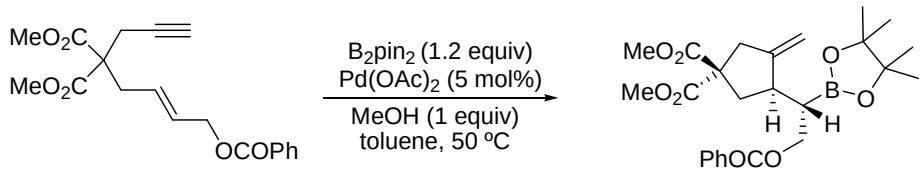


Figure 5. *X-ray diffraction structure from benzoate derivative* ***2b***.

With the aim of study the stereoespecificity of the process, the *E* isomers of **1a** and **1b** were prepared. Thus, when the reaction was performed with **(*E*)-1a** and **(*E*)-1b** the correspondent diastereomers of **2a** and **2b** were afforded (**2a'** and **2b'**, respectively) in low yield and mixed with non-separable impurity. And, by this way demostrating that the process takes place in a stereoespecific way (*Scheme 4*).

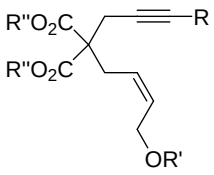
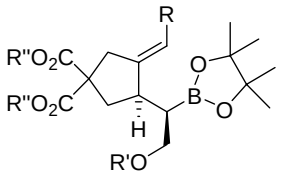


(*E*)-1a : R = Me
(*E*)-1b : R = Ph

2a' : R = Me
2b' : R = Ph

Scheme 4. *E-enynes and demostration of the stereoespecificity.*

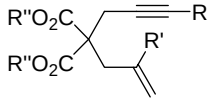
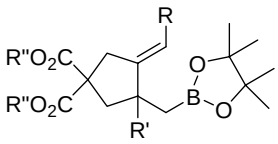
Considering the better yields resulting from the reaction with allylic acetates containing internal alkynes (entries 3-5, *Table 1*), the preparation of the analogous allylic ethers, as possible coordinating group bearing an internal alkyne, **1f-i**, was approached. Indeed, these substrates led, under optimized conditions, to the alkylboronates, **2f-i**, with excellent yields (*Table 2*).

	substrate	time (h)	product	yield (%)
				
1	**1f**	24[a]	**2f :** R = Me, R' = Me, R''= Et	80
2	**1g**	4	**2g :** R = Me, R' = CH_2Ph, R''= Et	93
3	**1h**	3	**2h :** R = Ph, R' = Me, R''= Me	77
4	**1i**	3	**2i :** R = Ph, R' = CH_2Ph, R''= Me	71

[a] Additional $Pd(OAc)_2$ (5 mol%) and MeOH (1 equiv) were added after 9 h.

Table 2. *Alkylboronates from allylic ether derivatives.*

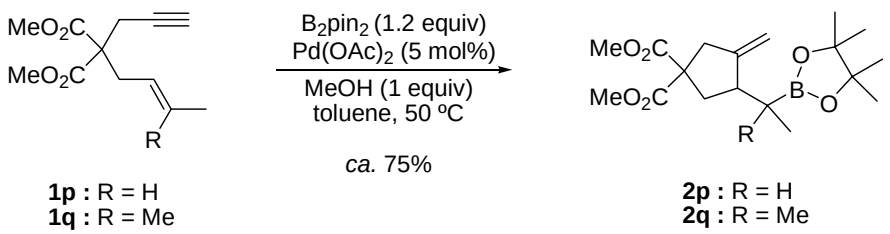
Furthermore, the reaction was carried out with substrates that contain non-coordinating groups on the allylic position, **1j-o**. Even substrates containing *β*-hydrogens susceptible of elimination afforded the expected boronates in good to excellent yields (entries 2-4, *Table 3*). This fact significantly widens the reaction scope. Compounds **1n** and **1o** led, however, to considerable lower yields.

	substrate	time (h)	product	yield (%)
				
1	**1j**	3	**2j :** R = H, R' = Me, R'' = Me	75
2	**1k**	3.5	**2k :** R = H, R' = H, R'' = Me	78
3	**1l**	6	**2l :** R = Me, R' = H, R'' = Et	93
4	**1m**	70[a]	**2m :** R = Ph, R' = H, R'' = Me	86
5	**1n**	4.5	**2n :** R = CO_2Me, R' = H, R'' = Me	43
6	**1o**	5	**2o :** R = H, R' = CH_2SO_2Ph, R'' = Me	31

[a] Additional $Pd(OAc)_2$ (5 mol%) and MeOH (1 equiv) were added after 23 h.

Table 3. *Alkylboronates from enynes with non-coordinating groups.*

In relation to this type of substrates, crotyl and prenyl derivatives (**5** and **6**, *Scheme 5*) were also tested under optimized conditions. Both compounds led to the corresponding alkylboronates in good yields (*ca.* 75%). Yields were determined by ^{1}H-NMR since the corresponding alkylboronates were obtained as a mixture of non-separable products, probably coming from *β*-elimination processes.

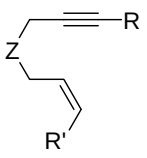
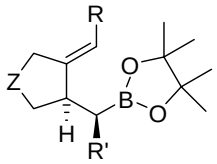


1p : R = H
1q : R = Me

2p : R = H
2q : R = Me

Scheme 5. *Other non-coordinating enynes.*

Apart from the examples previously showed, in which the atom-bridge moiety was always a malonate derivative, compounds containing other groups such as amide, ether, methylene or bis(sulfonyl)methane were also tested under the reaction conditions (**1p-t**). In all cases alkylboronates were obtained in low to moderate yields (*Table 4*).

	substrate	time (h)	product	yield (%)
				
1	**1r**	2.5	**2r :** Z = NTs, R = H, R' = CH_2OAc	30
2	**1s**	84[a]	**2s :** Z = O, R = Me, R' = CH_2OAc	21[b]
3	**1t**	20	**2t :** Z = CH_2, R = H, R' = H	14
4	**1u**	3	**2u :** Z = $C(SO_2Ph)_2$, R = H, R' = CH_2OAc	47
5	**1v**	5	**2v :** Z = $C(SO_2Ph)_2$, R = H, R' = CH_2OBz	47

[a] Additional $Pd(OAc)_2$ (5 mol%) was added after 21 h.

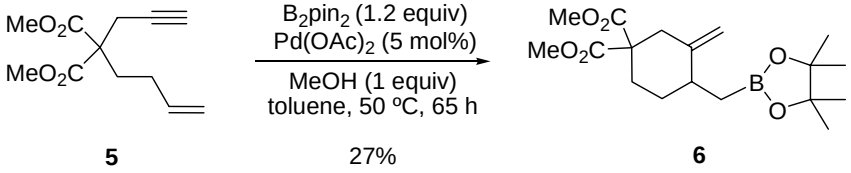
[b] Only 68% conversion was observed. Oligomers from **1s** seem to be formed.

Table 4. *Alkylboronates from non-malonate atom-bridge derivatives.*

Probably, these low results are due to a decrease of the *gem*-disubstituted effect (also named Ingold-Thorpe effect or angle compression).[246] According to this effect, two bulky subtituents on a tetrahedral center increase the angle between them. As a result, the angle between the other two substituents decreases. Therefore, the cyclization reactions are accelerated since the two reactive insaturated moieties are closer. Thereby, ether, amide of methylene groups at the atom-bridge moiety confer more flexibility to the molecule placing the alkyne and alkene moieties remote to each other (entries 1-3, *Table 4*). However, in the case of bis(sulfonyl)methanes, the steric hindrance enhances the reaction rate which lead to moderated yields (entries 4 and 5, *Table 4*). Moreover, possible interactions between the catalytic species and heteroatomic groups (O, N, S) could also contribute to the low yields.

[246] (a) Beesley, R. M.; Ingold, C. K.; Thorpe, J. F. *J. Chem. Soc., Trans.* **1915**, *107*, 1080-1106. (b) Jung, M.; Piizzi, G. *Chem. Rev.* **2005**, *105*, 1735-1766.

The reaction was extended to 1,7-enynes. Whereas 1,6-enynes always afforded five-membered rings alkylboronates, the 1,7-enyne **5**, homologous to **1k**, led to the six-membered ring alkylboronate **6** in low yield (27%) with only 80% conversion after 65 h (*Scheme 6*).



***Scheme 6**. 1,7-Enyne borylative cyclization.*

The reaction of enyne **1l** was also tested in the presence of bis(catecolato)diboron, instead of bis(pinacolato)diboron (entry 3, *Table 3*, 93%). In this case ^{1}H-NMR spectra of the crude showed the expected catecol-alkylboronate derivative. However, this resulting boronate seems unstable to air and its complete decomposition was finally observed when its isolation was tried by silica gel chromatography.

In regard to the results obtained until this moment, some considerations can be emphasized. For instance, those entries showing yields higher than 80% (*Table 1*: 3 and 4; *Table 2*: 1 and 2; *Table 3*: 3 and 4), involve enynes containing an internal alkyne and a malonate derivative at the atom-bridge moiety, regardless of the substitution on the allylic position. By other side, it is noteworthy that the new exocyclic double bond formed in the alkylboronate always shows the *E* configuration.

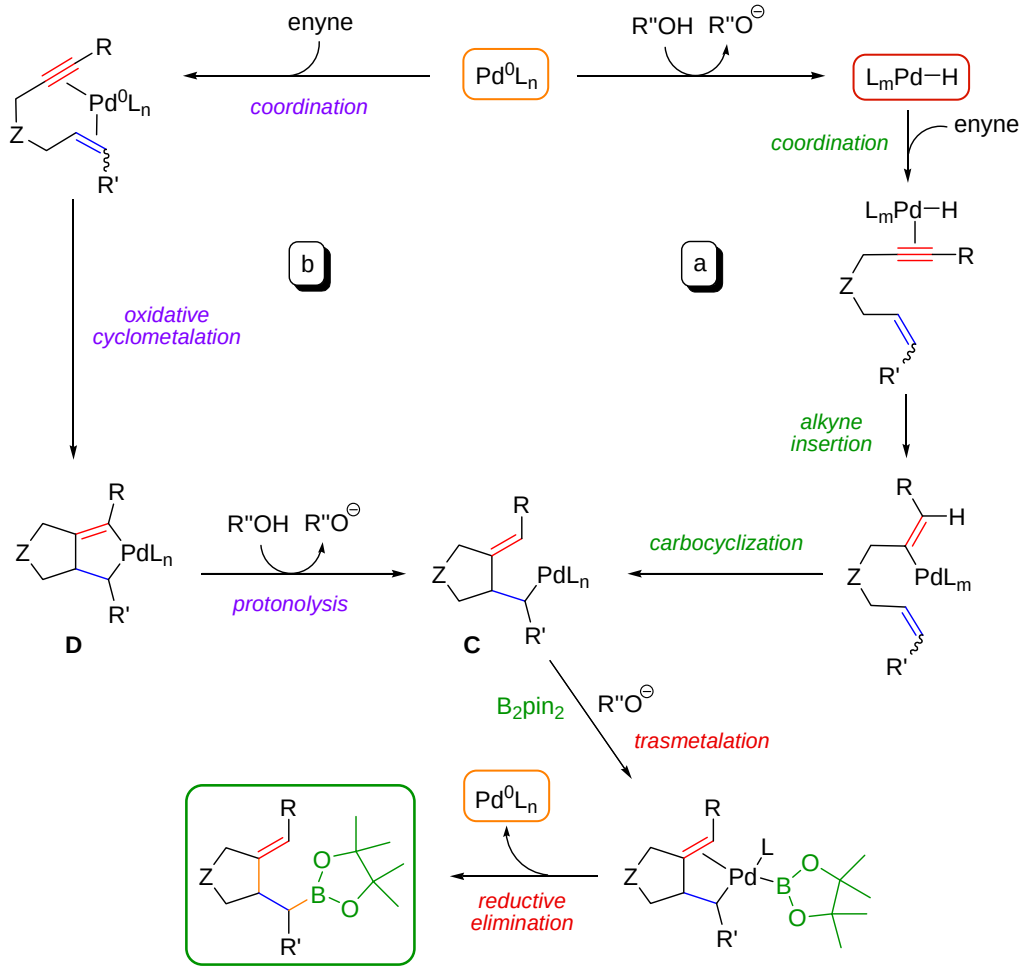
In accordance with all these observations and with the results of the experiments, a feasible mechanistic course could be proposed (*Scheme 7*).

First of all, reduction of precatalyst affords catalytically active Pd(0) species in the reaction mixture. This reduction of $Pd(OAc)_2$ to Pd(0) is a facile process that may be promoted by β-elimination from the acetate ligand or the alcohol, or by double transmetalation from bis(pinacolato)diboron. Other approaches such as oxidative addition of bis(boronates) to Pd(0) or metathesis with Pd-alkyne complexes has been calculated to be disfavored.[247] Therefore, these alternatives do not seem probable.

Instead, formation of a Pd hydride by protonation with the alcohol followed by insertion of the alkyne into de Pd–H bond would account for the observed alkene stereochemistry

[247] Cui, Q.; Musaev, D. G.; Morokuma, K. *Organometallics* **1998**, *17*, 1383-1392.

(*Scheme 7*, pathway *a*).[a] Next, carbocyclization process with the pendant alkene give rise to the key alkylpalladium intermediate **C**.



***Scheme 7**. Proposed mechanistic pathways.*

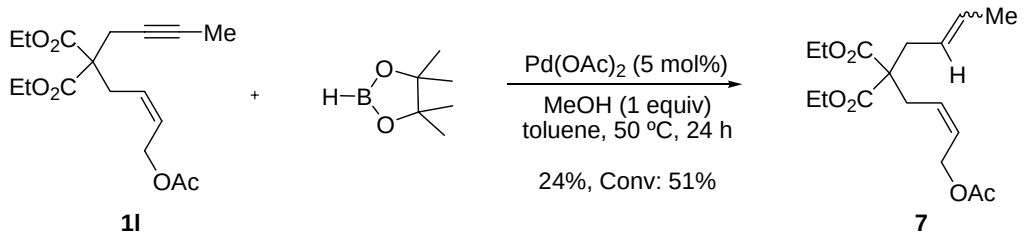
Alternatively, intermediate **C** could be formed by sequential coordination of the enyne to Pd(0), oxidative cyclometalation to give metalacycle **D**, and subsequent protonolysis of the Pd-C(sp2) bond (*Scheme 7*, pathway *b*).[b]

Both mechanistic possibilities are consistent with the stereochemistry of the new stereogenic centers. Nevertheless, previous calculations showed a high activation energy for the oxidative cyclometalation of enynes.[248]

Furthermore, intermediacy of pinacolborane can be discarded as intermediate since reaction of **1c** with H–Bpin instead of B_2pin_2 in the same conditions for 24 h only

[137] (a) Oh, C. H.; Jung, H. H.; Kim, K. S.; Kim, N. *Angew. Chem., Int. Ed.* **2003**, *42*, 805-808.
[143] (b) Trost, B. M.; Toste, D. F.; Pinkerton, A. B. *Chem. Rev.* **2001**, *101*, 2067-2096.
[248] Martín-Matute, B.; Buñuel, E.; Méndez, M.; Nieto-Oberhuber, C.; Cárdenas, D. J.; Echavarren, A. M. *J. Organomet. Chem.* **2003**, *687*, 410-419.

afforded alkyne hydrogenation derivatives (24% yield) with low conversion (51%) (*Scheme 8*).



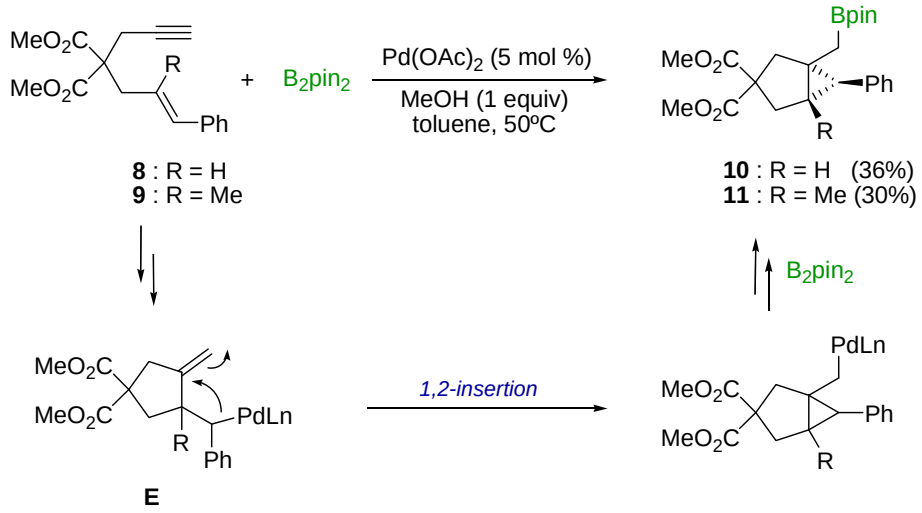
Scheme 8. *Reaction using H–Bpin instead of B_2pin_2.*

Finally, transmetalation of **C** with bis(pinacolato)diboron promoted by alkoxide followed by reductive elimination would give the final product and regenerate the Pd(0) catalyst (*Scheme 7*).

It is important to note that transmetalation seems to be faster than *β*-hydride elimination. Probably, in the "ligandless" conditions in which the reaction takes place, intramolecular coordination of the alkene in intermediate **A** prevents the adoption of the required conformation for this elimination to take place. This fact contrasts with Suzuki cross-coupling reactions of substrates containing *β*-hydrogens which have been achieved by a precise control of the electronic and steric properties of phosphine ligands.[249] Other possibility when phosphine ligands are added to the reaction mixture is the presence of these species coordinating to the Pd in the intermediate **A**. This fact could avoid the approximation of the bis(pinacolato)diboron to the reaction center and by this way turning to the *β*-elimination in almost exclusive process.

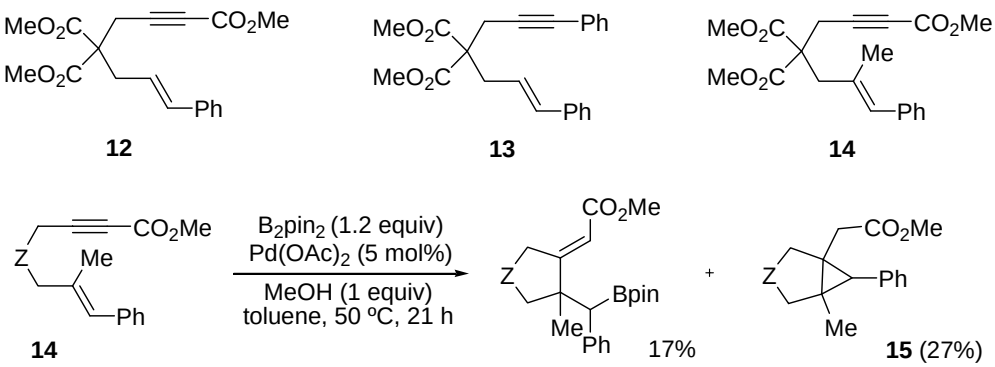
Interestingly, aryl alkenes **8** and **9** gave cyclopropyl derivatives **10** and **11**, respectively although in low yields (*Scheme 9*). An explanation of the mechanism is a migration of the metal atom in the homoallylic system by 1,2-insertion in intermediate **E**.

[249] Netherton, M.; Dai, C.; Neuschütz, K.; Fu, G. C. *J. Am. Chem. Soc.* **2001**, *123*, 10099-10100.



Scheme 9. *Formation of cyclopropyl alkylboronate derivatives.*

It is important to note that in both cases (**8** and **9**) phenyl groups located in *trans* position are invoked. However, not only Ph groups, when the reaction was performed with other *E* enynes such as (*E*)-**1a**, (*E*)-**1b**, **1p**, and 1**q**, minor compounds that impurify the alkylboronates seem to be cyclopropyl derivatives and/or *β*-elimination compounds. In order to obtain more information about this process, some subtrates with *trans* phenyl groups and substituted on the alkyne moiety were prepared (**12**, **13**, and **14**, *Scheme 10*), which could facilitates the isolation. The presence of an electron-withdrawing group on the alkyne should favour the "nucleophilic attack" of the alkylpalladium intermediate **E** (*Scheme 9*) into the exocyclic alkene. Nevertheless, when the reaction of **12** and **14** took place under optimized conditions a mixture of corresponding alkylboronate of type **2**, a cyclopropyl derivative that did not incorporate the boronate moiety and a small quantity of *β*-elimination compounds were obtained. Whereas, in the case of **13**, the starting enyne was almost totally recovered.



Scheme 10. *Other trans-phenyl enynes and formation of cyclopropyl derivatives.*

In the case of **14**, alkylboronate of type **2** and cyclopropyl derivative **15** could be separated in low yields and suitable crystals for X-ray diffraction were obtained from **15** (*Figure 6*). Same reaction was tested in absence of B_2pin_2 and the starting enyne **14** was almost completely recovered with no significative signals of cyclopropyl formation according to the ^{1}H-NMR spectra.

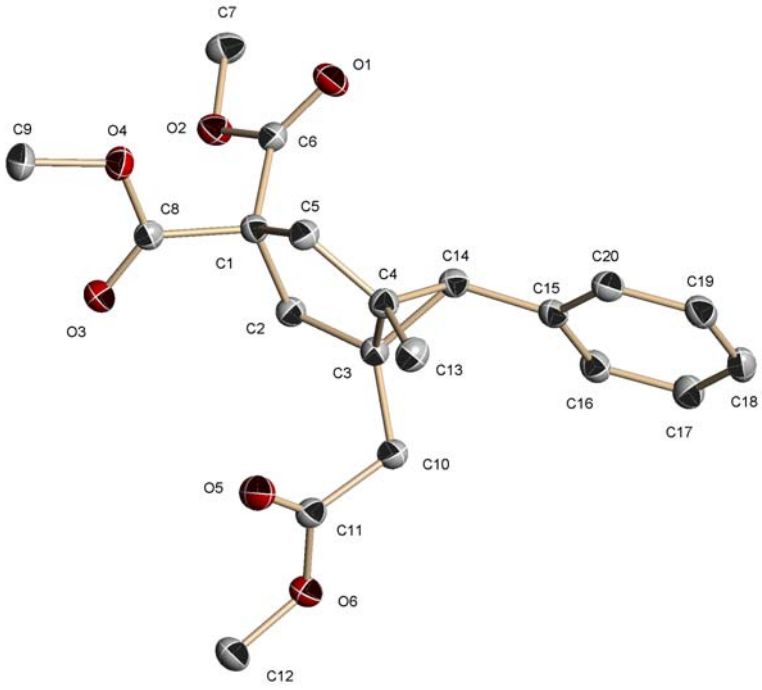
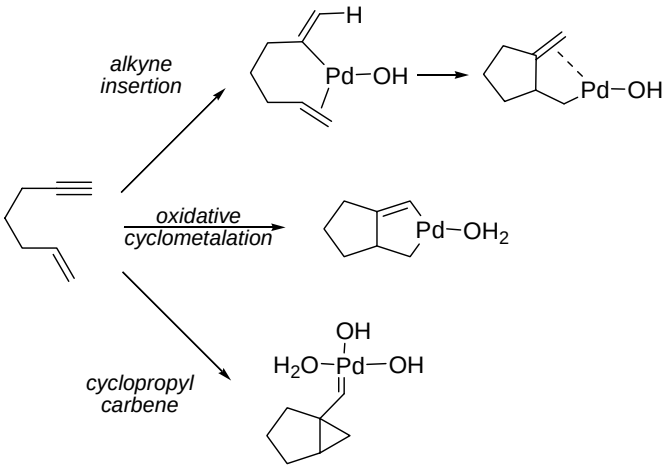


***Figure 6**. X-ray diffraction structure from cyclopropyl derivative **15**.*

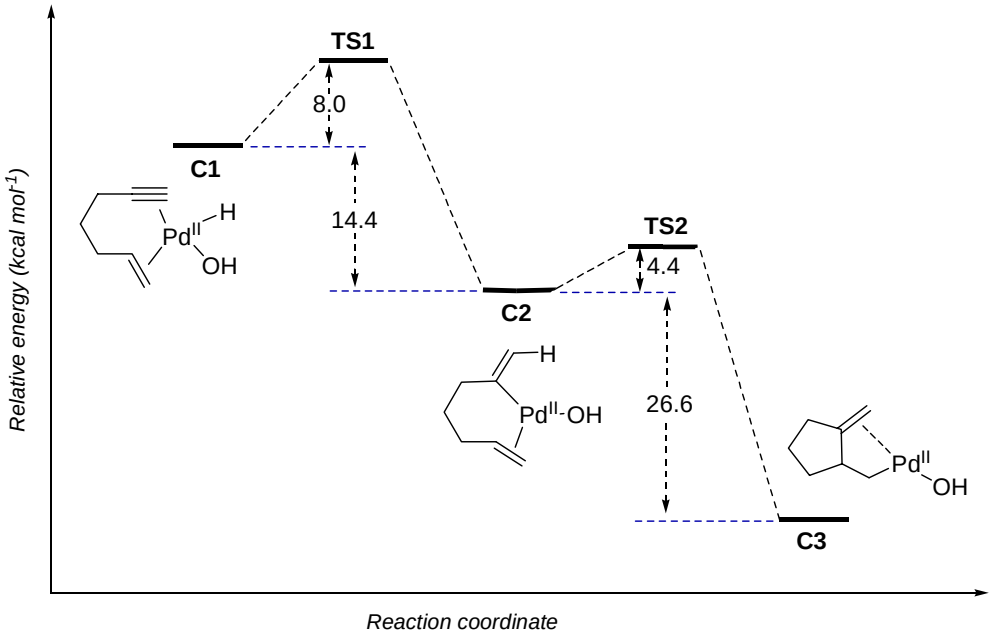
The synthesis of these type of cyclopropyl compounds suggested an alternative to the proposed mechanism pathways, being possible the presence of cyclopropyl carbene species involved in the formation of compounds **2**.

In order to obtain mechanistic insights, computational calculations were performed with Gaussian 03 at DFT level (see *Appendix I: Computational Section*). Thereby, and taking account the reaction products, three different pathways were studied (*Scheme 11*): insertion of the alkyne into a previously formed Pd–hydride, oxidative cyclometalation, and formation of cyclopropyl carbene species.



Scheme 11. *Three possible mechanistic pathways.*

Note that for all the calculations Pd-complex models were structurally simplified bearing hydroxy groups as the ligands, intead of methoxy or acetoxy groups, in order to facilitate computational study.

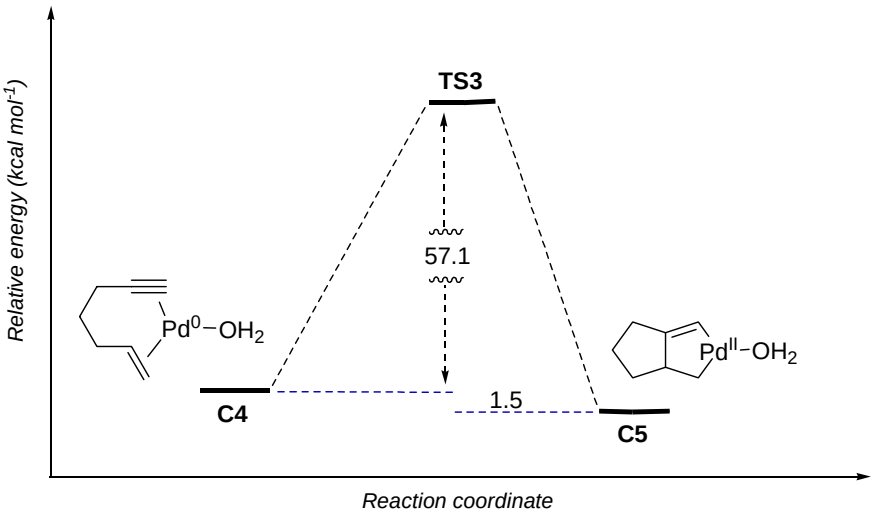


Scheme 12. *Alkyne insertion into Pd-hydride. B3LYP/6-31G(d) (C, H, O), LANL2DZ (Pd); Δ(E+ZPE) is given in kcal mol*$^{-1}$ *(gas-phase).*

Considering the mechanistic pathway involving Pd-hydride species, alkyne insertion would start from the Pd(II)-hydride complex (**C1**), in which the metal is coordinated to both insaturated moeities of the enyne (*Scheme 12*). This complex **C1** would suffer the

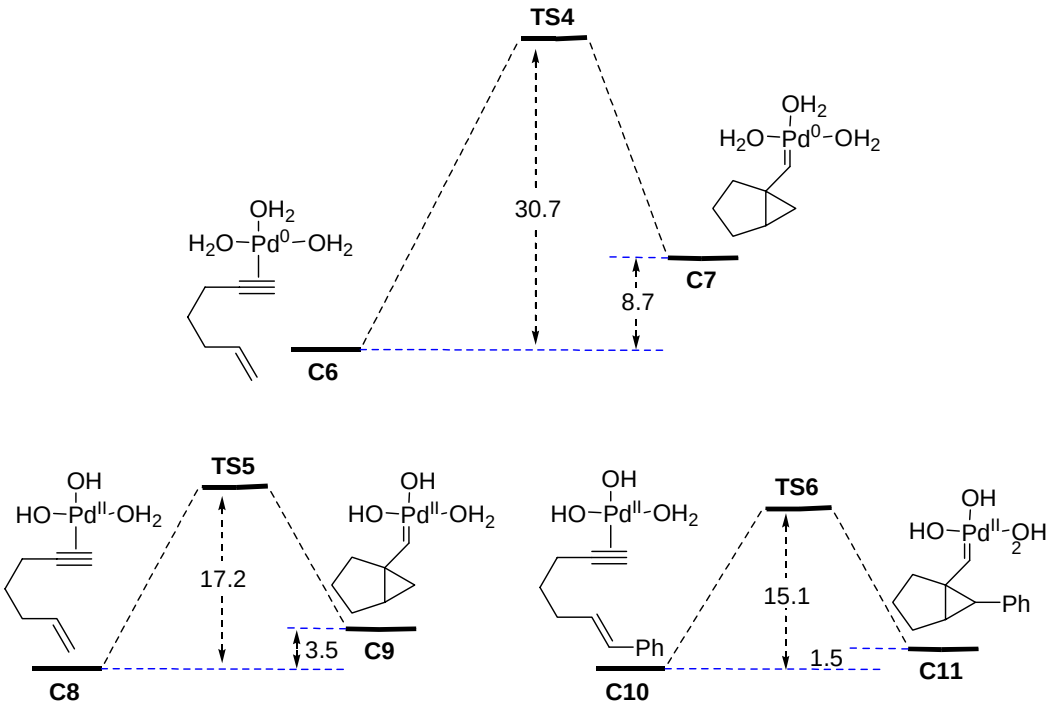
insertion of the alkyne moiety through a transition state **TS1** leading to the alkenyl-Pd complex **C2** with an activation energy of 8.0 kcal mol-1 and exotermically (-14.4 kcal mol-1). Then, alkenyl-Pd complex **C2** would evolve by carbometalation, through **TS2** (4.4 kcal mol-1), to afford the final alkyl-Pd complex **C3** also through an exotermic step (-26.6 kcal mol-1). It is important to note that the global process is highly exotermic (-41.0 kcal mol-1).

On the other hand, to study the cyclometallative oxidation approach (*Scheme 13*), a Pd(0) complex (**C4**) was selected. In this case the formation of cyclopalladation complex **C5** would take place through a transition state **TS3** with a high activation energy (57.1 kcal mol-1), which points to a much less feasible process, compared to the alkyne insertion into the Ph-hydride, that could be ruled out.



Scheme 13. *Oxidative cyclometalation. B3LYP/6-31G(d) (C, H, O), LANL2DZ (Pd); Δ(E+ZPE) is given in kcal mol-1 (gas-phase).*

As above mentioned, third possibility considered was the formation of a Pd-cyclopropyl carbene complex. For this approach two Pd-complexes containing the metal in two different oxidation states, Pd(0) and Pd(II), were analyzed (*Scheme 14*). In the case of Pd(0)-complex **C6**, Pd-cyclopropyl carbene complex **C7** was achieved throught **TS4** (30.7 kcal mol-1) in an endotermic process (8.7 kcal mol-1). Instead, Pd(II) complex **C8** led to the correspondent cyclopropyl carbene **C9** with a notably lower activation energy (**TS5**, 17.2 kcal mol-1) and endotermically (3.5 kcal mol-1).

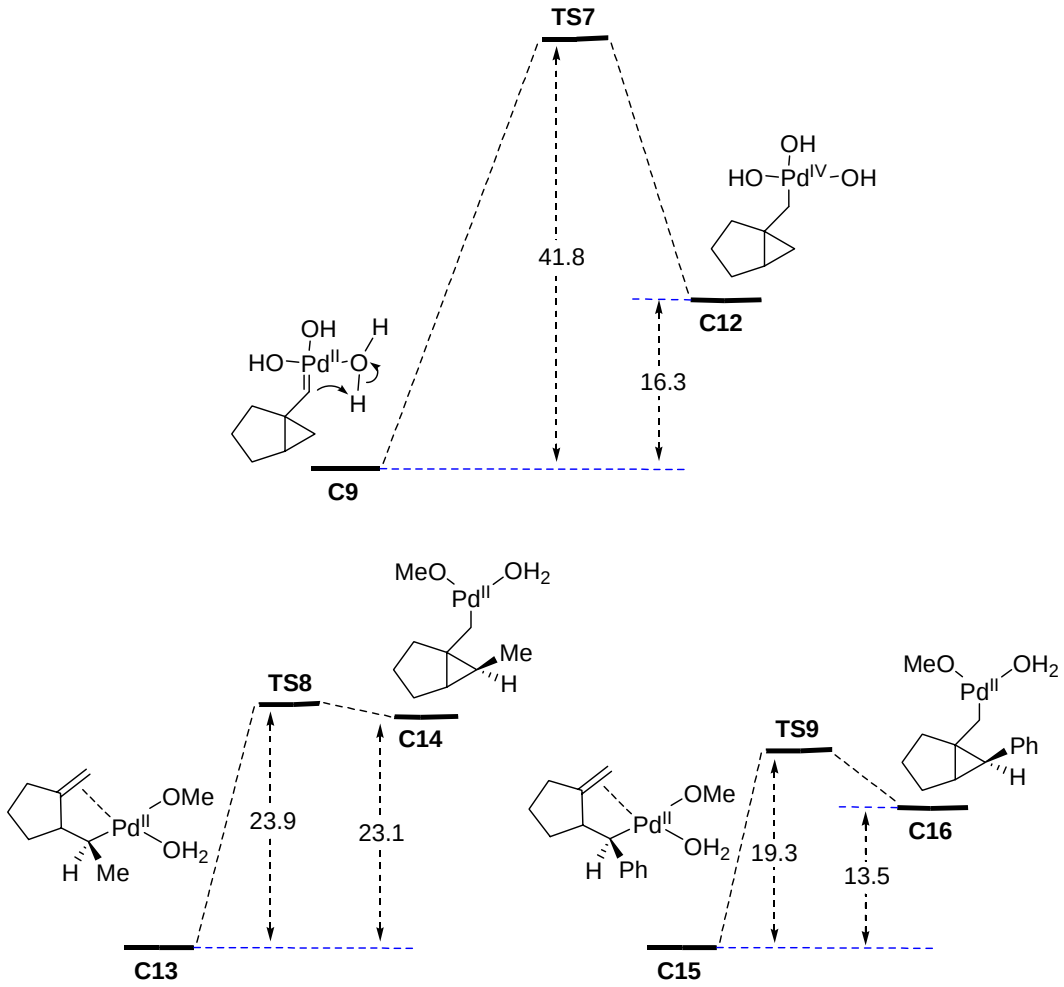


Scheme 14. *Cyclopropyl carbenes. B3LYP/6-31G(d) (C, H, O), LANL2DZ (Pd); Δ(E+ZPE) is given in kcal mol^{-1} (gas-phase).*

Since the cyclopropyl derivatives could be isolated when a phenyl group was located in the alkene adquiring *trans* configuration, a Pd(II)-model with this group and geometry for double bond was used (**C10-TS6-C11**, R = Ph). Nevertheless, similar energy date were obtained compared to **C8-TS5-C9** (R = H) (*Scheme 14*).

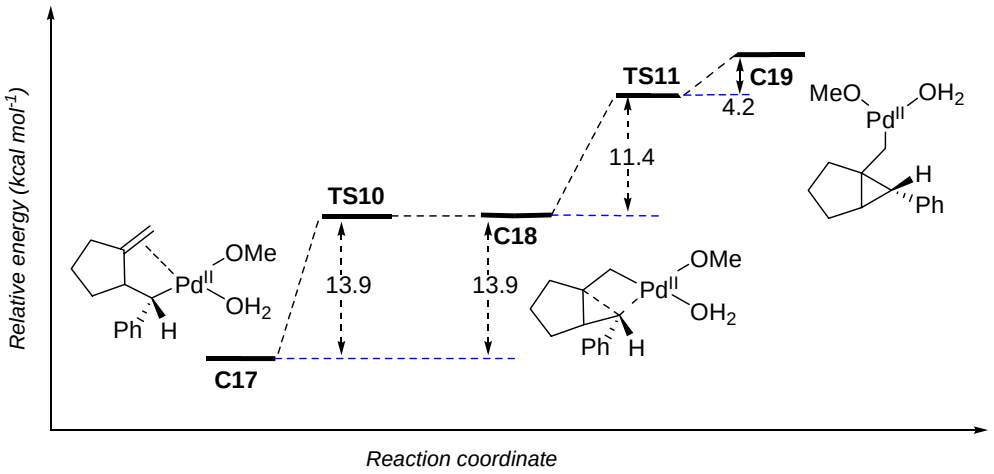
Therefore, with these results, alkyne insertion into the Pd-hydride seems to be the most feasible way, considering a lower activation energy and much higher stability of the final complex (*Scheme 12*).

On the other hand, and in order to clarify the mechanistic process for the formation of cyclopropyl derivatives, two different pathways were considered, evolution of a Pd(II)cyclopropyl carbene type of **C9** or, the 1,2-insertion of exocyclic double bond into a Pd–C bond of an alkyl-Pd complex similar to **C3**. In the first case, Pd(II)-cyclopropyl carbene complex **C9** would lead to the cyclopropyl alkyl-Pd complex **C12** with a high activation energy (**TS7**, 41.8 kcal mol-1) following a Pd(II)-Pd(IV) endotermic process (16.3 kcal mol-1) (*Scheme 15*).



Scheme 15. *Formation of cyclopropyl derivatives. B3LYP/6-31G(d) (C, H, O), LANL2DZ (Pd); Δ(E+ZPE) is given in kcal mol^{-1} (gas-phase).*

In contrast, the insertion of alkene in an alkyl-Pd complex, derived from an enyne with *E* configuration (**C13**, R = Me; or **C5**, R = Ph), would proceed through a lower activation energy in both cases (**TS8**, 23.9 kcal mol-1; and **TS9**, 19.3 kcal mol-1, respectively) and also in a endotermic manner (*Scheme 15*). In addition, when an alkyl-Pd complex formed from an enyne with the opposite configuration (**C17**) was used, the process took place in two steps through the formation of alkyl-Pd complex intermediate **C18**, although with similar energy in the global process (*Scheme 16*).

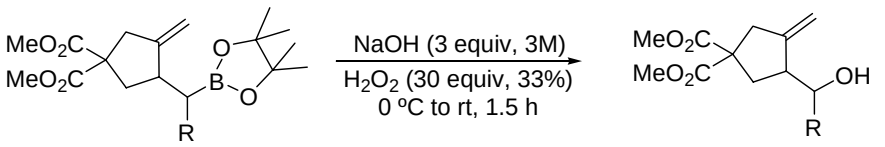


Scheme 16. *Formation of cyclopropyl derivatives. B3LYP/6-31G(d) (C, H, O), LANL2DZ (Pd); Δ(E+ZPE) is given in kcal mol*$^{-1}$ *(gas-phase).*

In conclusion, alkyne insertion approach seems to explain the formation of the products showing lower activation energies, and by this way supporting the proposed mechanism.

With the aim of enhance the proyection of the new reaction and the applicability of the synthesized alkylboronates, some functionalization methods such as oxidation to alcohols or Suzuki coupling to form new C-C bonds were approached.

Oxidation processes were performed with alkylboronates **2b** and **2k** under alkaline aqueous conditions[91b] in the presence of a large excess of oxygen peroxyde (33% w/v). Thus, the correspondent alcohols **16** and **17** were obtained in high yields after an easy purification by sylica gel column chromatography (*Scheme 17*).



2b : R = CH_2OBz
2k : R = H

16 : R = CH_2OBz (84%)
17 : R = H (93%)

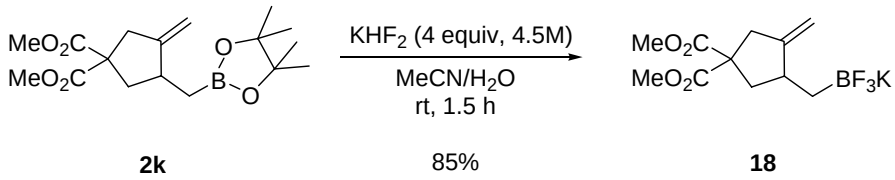
Scheme 17*. Formation of alcohols from alkylboronates.*

On the other hand, although several Suzuki coupling conditions were tested with alkylboronates, the coupling was not achieved since the use of C(sp^3)-B bonds in this

[91] (b) Snyder, H. R.; Kuck, J. A.; Johnson, J. R. *J. Am. Chem. Soc.* **1938**, *60*, 105-111.

type of coupling offers, very often, some unsolved problems, still remaining a challenge for the the cross-coupling reaction field.[108] However, other valid approximation to this objetive could be the transformation of the alkylboronates into the corresponding trifluoroborate salts.[35a,b] These salts have been demostrated to undergo Suzuki coupling with a large number of electrophiles, even regarless to the hybridation of the carbon involved in the reaction.

Thereby, alkylboronate **2k** was subjected to the trifluoroborate salt formation in the presence of a saturated aqueous solution of KHF_2 in acetonitrile at rt.[33] The borate salt **18** was obtained as a white solid in good yield (85%) after sucessive washes with diethyl ether (*Scheme 18*).



***Scheme 18**. Formation of alkytrifluoroborate salts.*

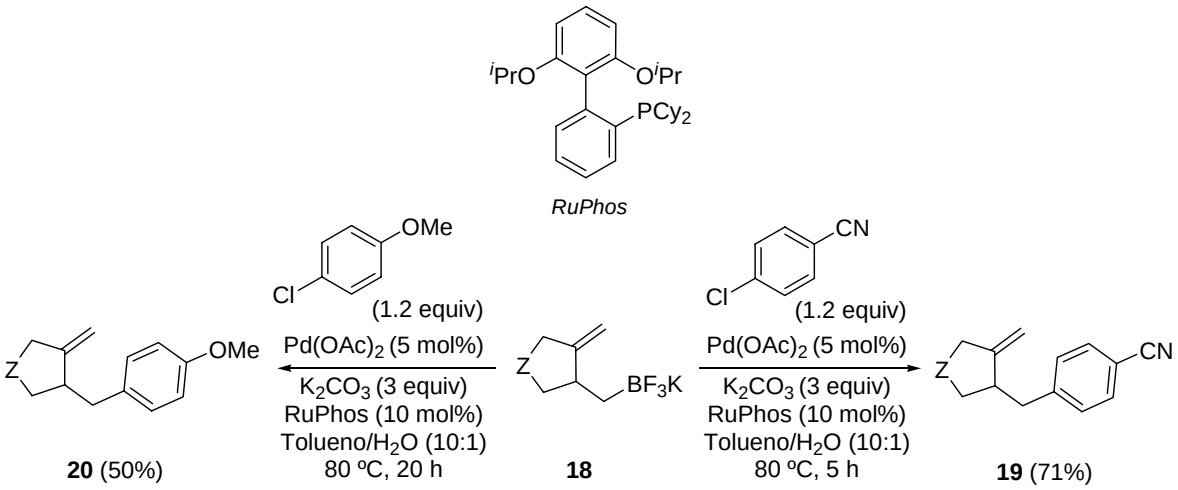
Under the reported conditions for the Suzuki coupling,[111] trifluoroborate salt **18** was coupled with aryl chorides, either with electron-withdrawing or electron-donor derivatives such as *p*-chlorobenzonitrile and *p*-chloroanisol, respectively. Thus, leading to the coupled products (**19** and **20**) with moderate to good yields (*Scheme 19*). The reason of choosing chlorine derivatives as C–C partners was their lower price and more availability than analogous bromine or iodine derivatives, although they are less reactive in the oxidative addition step of the the coupling process.

[33] (a) Vedejs, E.; Chapman, R. W.; Fields, S. C.; Lin, S.; Schrimpf, M. R. *J. Org. Chem.* **1995**, *60*, 3020-3027. (b) Vedejs, E.; Fields, S. C.; Hayashi, R.; Hitchcock, S. R.; Powell, D. R.; Schrimpf, M. R. *J. Am. Chem. Soc.* **1999**, *121*, 2460-2470.

[35] (a) Molander, G. A.; Ellis, N. *Acc. Chem. Res.* **2007,** *40*, 275-286. (b) Doucet, H. *Eur. J. Org. Chem.* **2008**, 2013-2030.

[108] Chemler, S. R.; Trauner, D.; Danishefsky, S. J. *Angew. Chem., Int. Ed.* **2001**, *40*, 4544-4568.

[111] Dreher, S. D.; Lim, S.-E.; Sandrock, D. L.; Molander, G. A. *J. Org. Chem.* **2009**, *74*, 3626-3631.



***Scheme 19**. Suzuki coupling of alkyltrifluoroborate salts.*

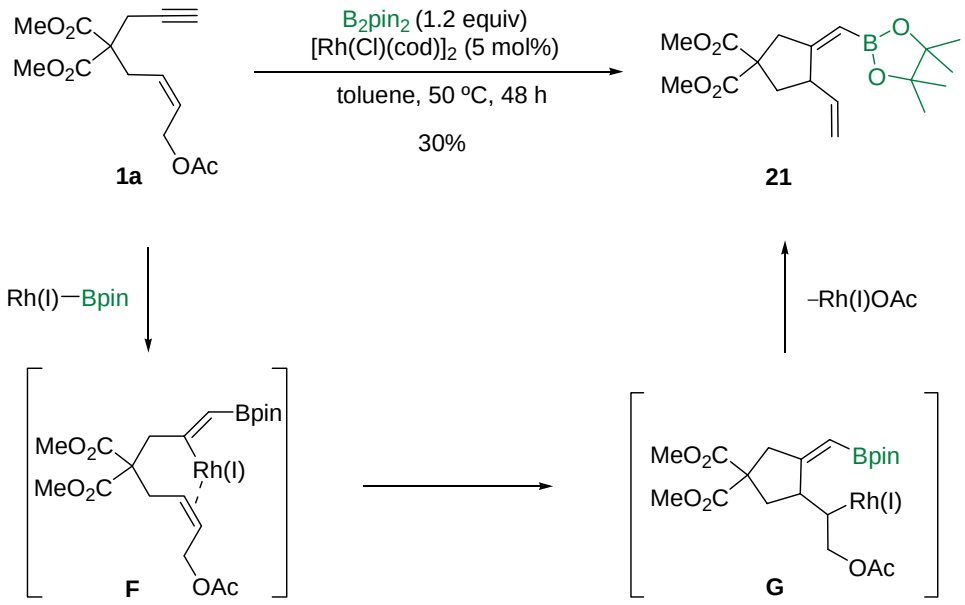
In summary, a new borylative cyclization reaction for the stereoselective synthesis of homoallylic alkylboronates has been developed in smooth conditions with a wide scope, since proceed with differently substituted alkenes and with both terminal and internal alkynes. Two new bonds, one C–C and one C–B, and two new asymmetric centers are formed stereospecifically. It tolerates the presence of *β*-hydrogens and avoids the use of highly nocleophilic reagents being compatible with a wide variety of functional groups. Moreover, some functionalizations of these derivatives has been achieved such as the formation of alcohols, alkyltrifluoroborate salts and C–C coupling products by Suzuki reaction.

Alternatively to the preparation of alkylboronates by this Pd-catalyzed borylative reaction and taking into account the work reported by Murakami and coworkers, in which Rh(I) species catalyzed the addition of aryl boronic acids to the cyclization of enynes,[211] the synthesis of alkenylboronates was approached. Similar alkenylboronates have been already described in the literature using cationic Rh-complexes as catalysts.[218]

The reaction was also carried out with allylic ether derivatives and dimeric Rh-complex $[Rh(OH)(cod)]_2$ under the optimized conditions reported by Murakami, however the best results were obtained starting from enyne **1a** (30%) in the presence of Rh dimeric complex $[Rh(Cl)(cod)]_2$ in tolene at 50 ºC.

[211] Miura, T.; Shimada, M.; Murakami, M. *J. Am. Chem. Soc.* **2005**, *127*, 1094-1095.
[218] Kinder, R., E.; Widenhoefer, R. A. *Org. Lett.* **2006**, *8*, 1967-1969.

The reaction is initiated by regioselective insertion of the alkyne into the B–Rh(I) bond, generated *in situ* by the transmetallation of Rh(I) with bis(pinacolato)diboron, affording the alkenyl-Rh(I) intermediate **F** (*Scheme 20*). Intramolecular carborhodation to the pendant allylic double bond then occurs in a 5-*exo* mode, leading to the formation of the alkyl-Rh(I) intermediate **G**. Finally, *β*-elimination of the acetate group affords the final alkenylboronate **21** with regeneration of a catalytically active Rh(I) species.



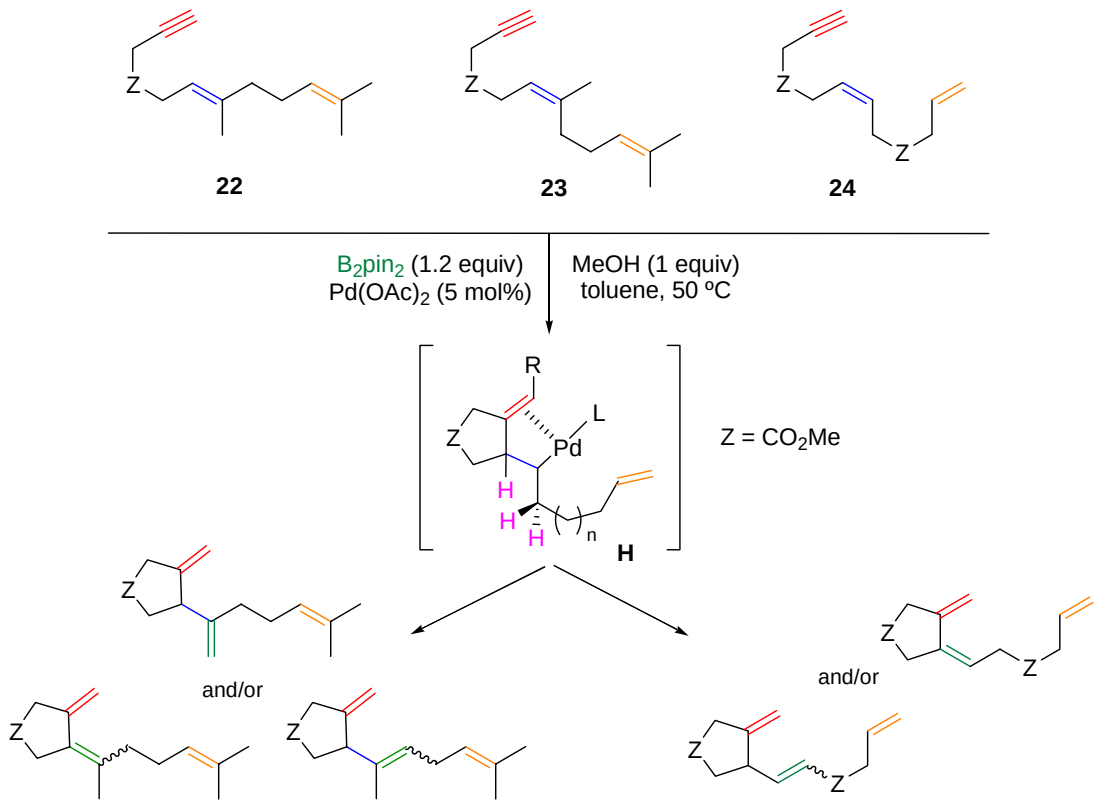
Scheme 20. *Rh-catalyzed synthesis of alkenylboronates.*

Unfortunately, efforts to increase the yield by addition of other species (catalysts, ligands, additives) or changing the solvents, did not afford better results. Probably the catalyst turn to inactive after some cycles since addition of higher catalyst quantities resulting in similar yields. Experiments for the optimization of this reaction are currently in progress.

2. Pd-Catalyzed Borylative Polycyclizations

With the aim to exploit the synthetic utility of the previously described new borylative/cyclization process, other more complex substrates that keep the enyne moiety were explore. Thereby, in order to build new substrates other insaturations were added to that enyne skeleton, such as double or triple bonds. The starting hypothesis was that species with three insaturations in the same molecule probably would lead to the formation of more than one cycle by trapping the alkylpalladium intermediate through these new insaturation moieties, in a single synthetic operation.

The main difference between our results compared to previous experiments carried out by Trost and coworkers[221] could be the incorporation of the boronate functionality after the polycyclization process in a tandem reaction.



Scheme 21. *Possible β-hydrogen elimination products obtained from dienynes.*

[221] (a) Trost, B. M.; Lee, D. C. *J. Am. Chem. Soc.* **1988,** *110,* 7255-7258. (b) Trost, B. M.; Lee, D. C. *J. Org. Chem.* **1989,** *54,* 2274-2275. (c) Trost, B. M.; Shi, Y. *J. Am. Chem. Soc.* **1993,** *115,* 12491-12509.

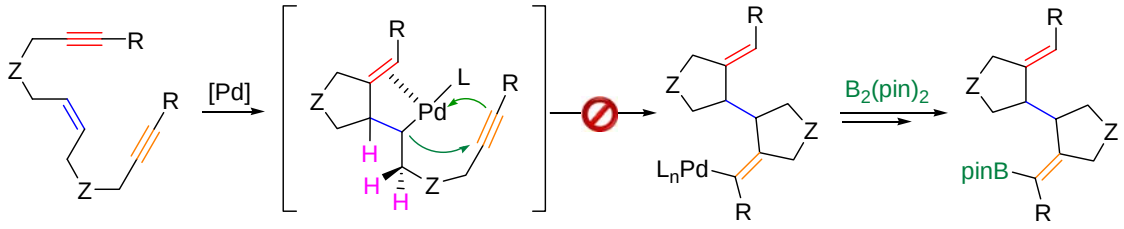
First of all, to the inicial malonate-based enyne, a geranyl (**22**), a neryl (**23**) and other allyl-malonate moiety (**24**) were linked looking for three different dienynes, where an additional alkene moiety constituted the initial polyunsaturated skeleton (*Scheme 21*). The three starting materials were reacted under optimized conditions, but only mixtures of non-separable *β*-hydrogen elimination products were obtained.

As previously mentioned, at the chapter related to 1,6-enynes, the success of the reaction relied on the absence of *β*-hydrogen elimination on the putative alkylpalladium intermediate. However, from these compounds, the second cyclization with the pendant alkene did not take place in **H** and the *β*-hydrogen elimination seemed to be the unique process.

Then, other possibilities for polycyclization of insaturated compounds were explored.

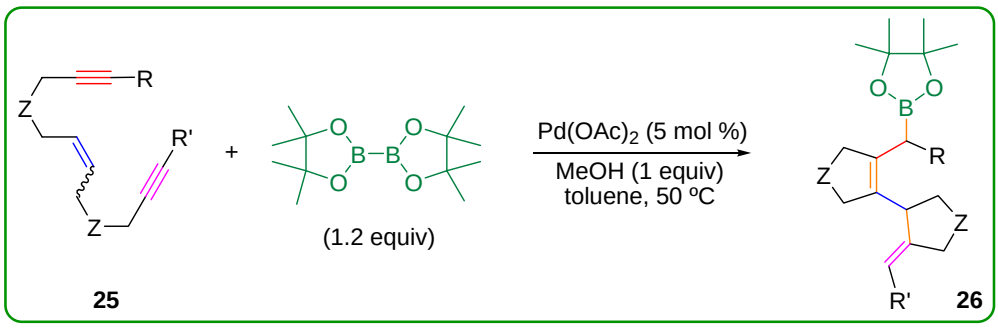
2.1 Pd-Catalyzed Borylative Bicyclization of 6-Ene-1,11-diynes to Allylboronates

Trapping the intermediate alkylpalladium resulting from a first cyclization, with a second alkyne was explored. This feasible process would give rise to alkenylpalladium complexes and, eventually, to alkenylboronates (*Scheme 22*).



Scheme 22. *Possible mechanistic pathway to alkenylboronates.*

Unexpectedly, when 6-ene-1,11-diyne **25** was reacted with bis(pinacolato)diboron in the presence of $Pd(OAc)_2$ and MeOH in toluene, allylboronate **26** was formed (*Scheme 23*).[250]



Scheme 23. *Pd-catalyzed bicyclization/borylation of 6-ene-1,11-diynes.*

In particular, this cascade reaction provided two C–C and one C–B bond and two new stereogenic centers in a single operation and stereoselectively.

The result was in sharp contrast with some results reported by Ojima, who obtained alkenylsilanes in a Rh-catalyzed hydrosilylilative cyclization of the same kind of enediynes.[229]

[229] (a) Ojima I.; McCullagh J. V.; Shay, W. R. *J. Organomet. Chem.* **1996**, *521*, 421-423. (b) Ojima, I.; Lee, S-Y. *J. Am. Chem. Soc.* **2000,** *122,* 2385-2386. (c) Bennacer, B.; Fujiwara, M.; Lee, S-Y.; Ojima, I. *J. Am. Chem. Soc.* **2005,** *127,* 17756-17767.

[250] (a) Marco-Martínez, J.; Buñuel, E.; Muñoz-Rodríguez, R.; Cárdenas, D. J. *Org. Lett.* **2008**, *10*, 3619-3621. (b) Marco-Martínez, J.; Buñuel, E.; Muñoz-Rodríguez, R.; Cárdenas, D. J. *Synfacts* **2008**, *10*, 1072-1072.

In order to study the scope of the process, the reaction was extended to a large number of related substrates, in which some modifications at the alkyne moieties of the enediyne were included. Thus, symmetrical and nonsymmetrical enediynes with *Z* configuration, and symmetrical enediynes with *E* configuration were prepared to test the reaction (*Figure 7*).

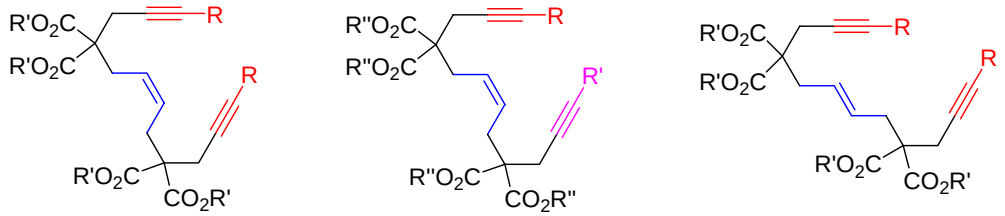
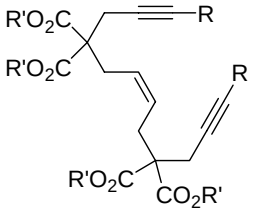
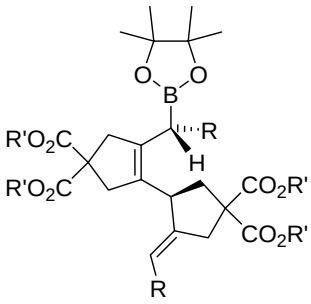


***Figure 7**. Modifications on the initial substrate.*

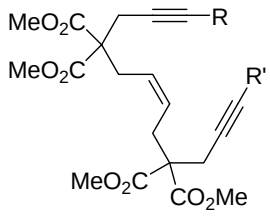
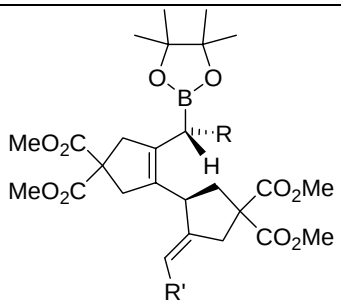
In the case of symmetrical (*Z*)-enediynes, the internal alkynes afforded the corresponding allylboronates in higher yields (entries 2-4, *Table 5*). Probably, the steric hindrance of these groups (Me, Ph, TMS) at the same carbon that the boronate functionality seems to prevent the boronate hydrolisis in the final product.

	substrate	time (h)	product	yield (%)
				
1	**(Z)-25a**	5.5	**26a :** R = H, R' = Me	38
2	**(Z)-25b**	7.5	**26b :** R = Me, R' = Me	83
3	**(Z)-25c**	7	**26c :** R = Ph, R' = Me	65
4	**(Z)-25d**	24	**26d :** R = $SiMe_3$, R' = Et	74[a]

[a] Related product with only one TMS group on the alkene was obtained in additional 5% yield (**26d'**, see experimental section).

***Table 5**. Allylboronates from symmetrical (Z)-enediynes derivatives.*

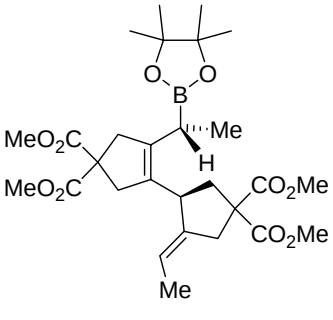
When the reaction was explored using nonsymmetrical (*Z*)-enediynes under the standard conditions the borylation of the terminal alkynes took place in a fully regioselective process (entries 1 and 2, *Table 6*). Once again, when both alkynes were subtituted (**(Z)-25g**) the yield enhanced, however a mixture of the two possible regioisomers was obtained.

	substrate	time (h)	product	yield (%)
				
1	**(Z)-25e**	4	**26e :** R = H, R' = Me	59
2	**(Z)-25f**	6	**26f :** R = H, R' = Ph	53
3	**(Z)-25g**	22	**26g :** R, R' = Ph, Me	72[a]

[a] Mixture of the two possible regioisomers (60:40). Major isomer: R = Ph, R' = Me.

***Table 6**. Allylboronates from nonsymmetrical (Z)-enediynes derivatives.*

The obtention of single crystals of allylboronate **26b** suitable for X-ray diffraction allowed the elucidation of the relative stereochemistry for the new stereogenic centers (*Figure 8*).



26b

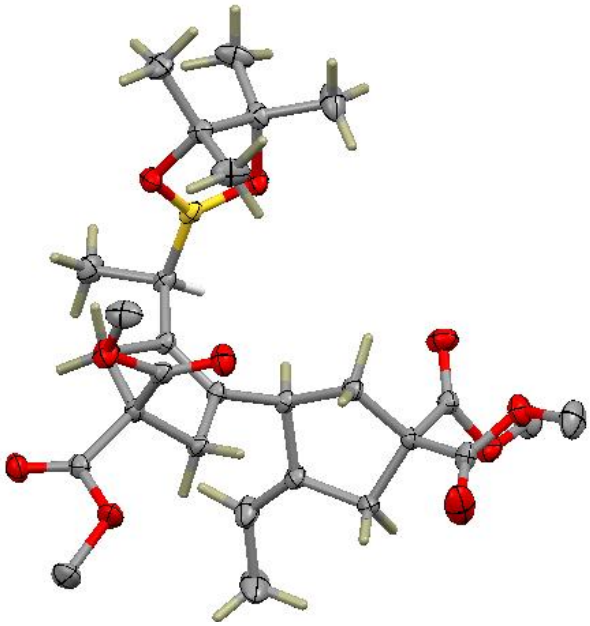
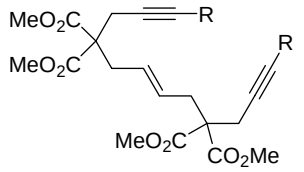
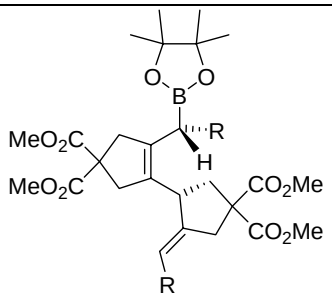


***Figure 8**. X-ray diffraction structure from allylboronate **26b**.*

Furthermore, the stereosespecifity of the reaction was confirmed by using symmetrical (*E*)-enediynes (*Table 7*), which provided different stereoisomers than obtained from analogous (*Z*)-enediynes. In this case, yields were lower due to the formation of unseparable dienes or tricycles, which difficult the isolation of the allylboronates.

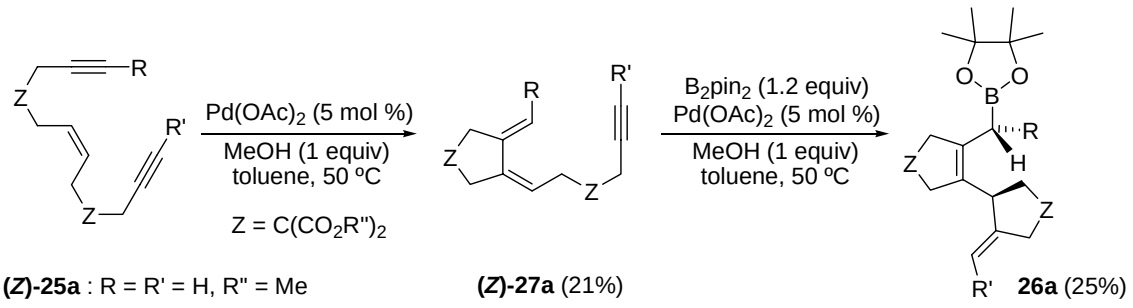
	substrate	time (h)	product	yield (%)[a]
				
1	**(*E*)-25a**	18	**26a :** R = H	36
2	**(*E*)-25b**	6	**26b' :** R = Me	70[b]
3	**(*E*)-25c**	7.5	**26c' :** R = Ph	46

[a] NMR yields in mixtures with dienes or tricycles.

[b] Reaction temperature: 70 ºC.

Table 7. *Allylboronates from symmetrical (E)-enediynes derivatives.*

With the aim of obtaining some evidence about the mechanism, enediynes were subjected to the reaction conditions in the absence of B_2pin_2. Thus, when the reaction took place with enediyne **(*Z*)-25a** the following diene **(*Z*)-27a** (R = H, 21%) was obtained stereoselectively (*Scheme 24*). Moreover, when that compound **(*Z*)-27a** was treated with B_2pin_2 and $Pd(OAc)_2$ under optimized conditions, the allylboronate **26a** was obtained in low yield (*ca.* 25%).[251] This fact strongly suggested the intermediacy of 1,3-dienes in the reaction pathway.



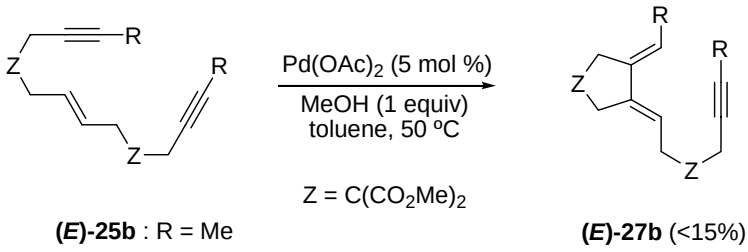
(*Z*)-25a : R = R' = H, R" = Me **(*Z*)-27a** (21%) R' **26a** (25%)

Scheme 24. *The reaction of Z-enediynes in the absence of B_2pin_2 affords 1,3-dienes* ***(Z)-27***.

[251] Approximate yield since starting diene **(*Z*)-27a** was not pure since these compounds tend to decompose and were difficult to purify.

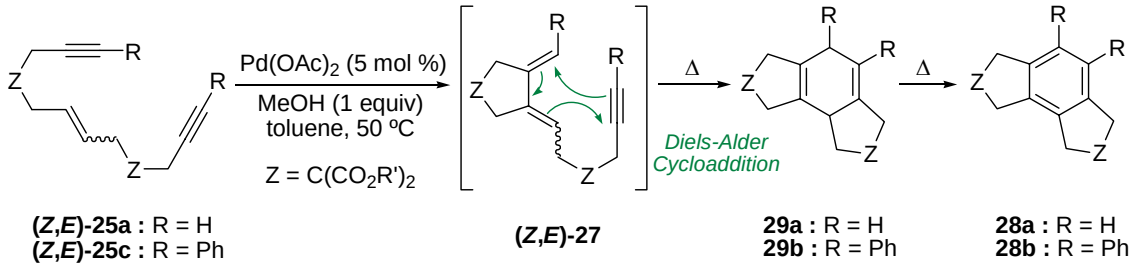
This experiment was also carried out with other symmetrical enediynes such as **(*Z*)-25b-d** leading to 1,3-dienes with the same double-bond configuration (confirmed by NOESY experiments). Although in low yields (< 35%), since in these cases partial decomposition of these compounds precluded isolating them in higher yields. By the same way, nonsymmetrical **(*Z*)-25e** and **(*Z*)-25f** gave the 1,3-dienes in a highly regioselective manner, since 1,3-dienes formed were almost exclusive obtained by the terminal alkyne moiety.

In contrast, the only product that could be isolated from the reaction of **(*E*)-25b** in the same conditions was the corresponding *E*-alkene **(*E*)-27b** (R = Me) which was consistent with a regio- and stereoselective *β*-hydrogen elimination (*Scheme 25*).



***Scheme 25**. The reactions of E-enediynes in the absence of B_2pin_2 affords 1,3-dienes **(E)-27**.*

On the other hand, reaction of *trans* derivative **(*E*)-25a** in the absence of B_2pin_2 led to tricycle **28a** (R = H) in 30% yield, instead of expected 1,3-diene that was no detected. Tricyclic compounds seem to be formed from compounds **27** by Diels-Alder intramolecular cycloaddition,[e, c] rather than coming from Pd-catalyzed reactions, since heating of **(*Z*)-27a** led to aromatized **28a** through the likely intermediacy of **29a** (R = H) (*Scheme 26*).



***Scheme 26**. Synthesis of tricyclic compounds by Diels-Alder intramolecular cycloaddition.*

[158] (e) Trost, B. M.; Tanoury, G. J.; Lautens, M.; Chan, C.; MacPherson, D. T. *J. Am. Chem. Soc.* **1994**, *116*, 4255-4267.

[221] (c) Trost, B. M.; Shi, Y. *J. Am. Chem. Soc.* **1993,** *115,* 12491-12509.

Moreover, diphenyl derivative **29b** (R = Ph) was isolated from **(*E*)-25c** from the reaction in the absence of B_2pin_2. This compound also aromatized to **28b** (R = Ph) upon heating a solution in the presence of oxygen, although more slowly. Probably, the steric hindrance between the phenyl rings precludes oxidation of the benzylic position in **(*E*)-25c**. Therefore, it is possible to conclude that the higher cycloaddition ability of **(*E*)-27** compared with **(*Z*)-27**, due to the configuration of the disubstituted alkene, explains why the former are not detected in some cases.

Single crystals suitable for X-ray diffraction were obtained from **28a**, **28b**, and **29b** (*Figure 9*). It is possible to appreciate the planarity in the case of aromatic compounds.

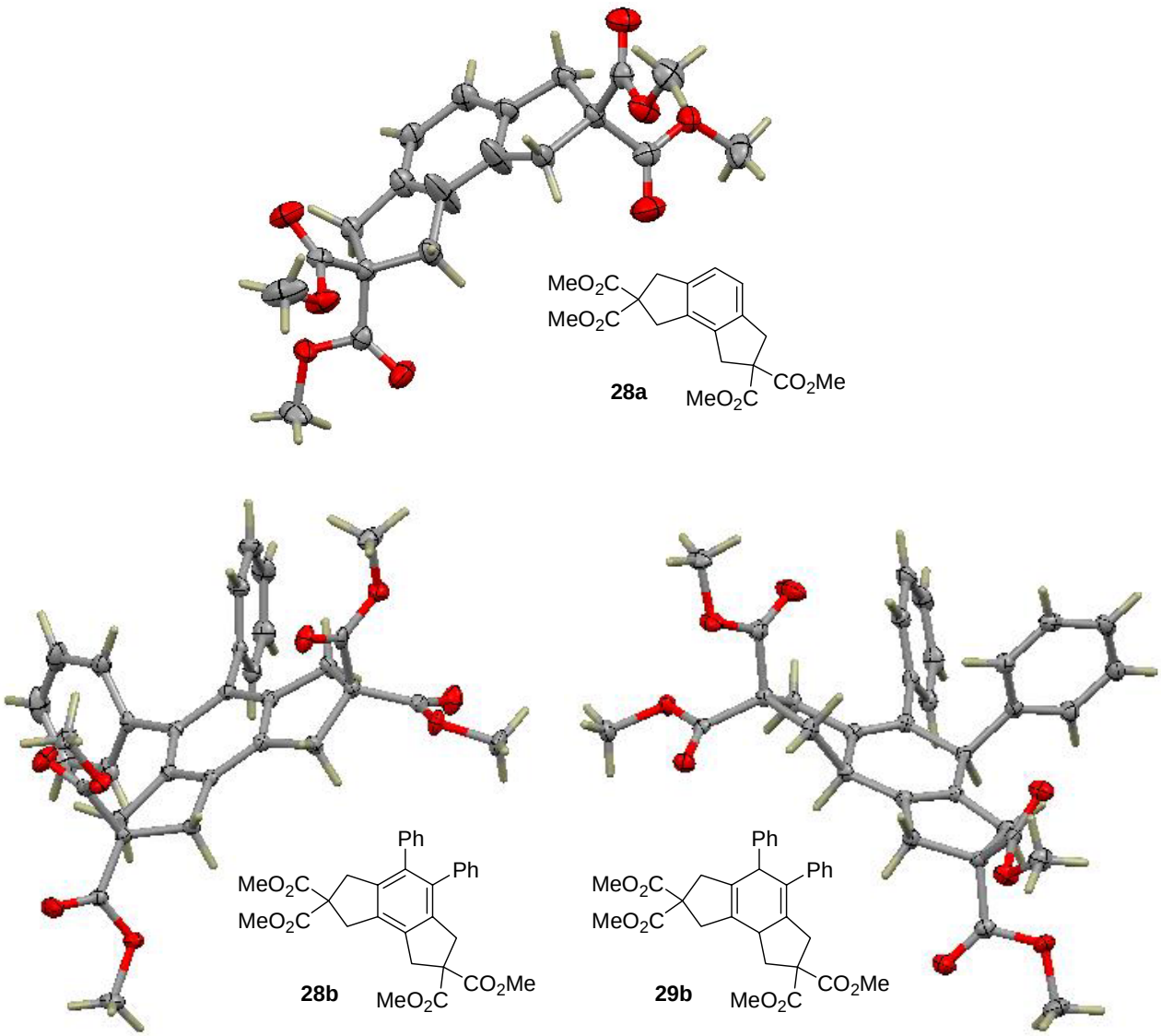
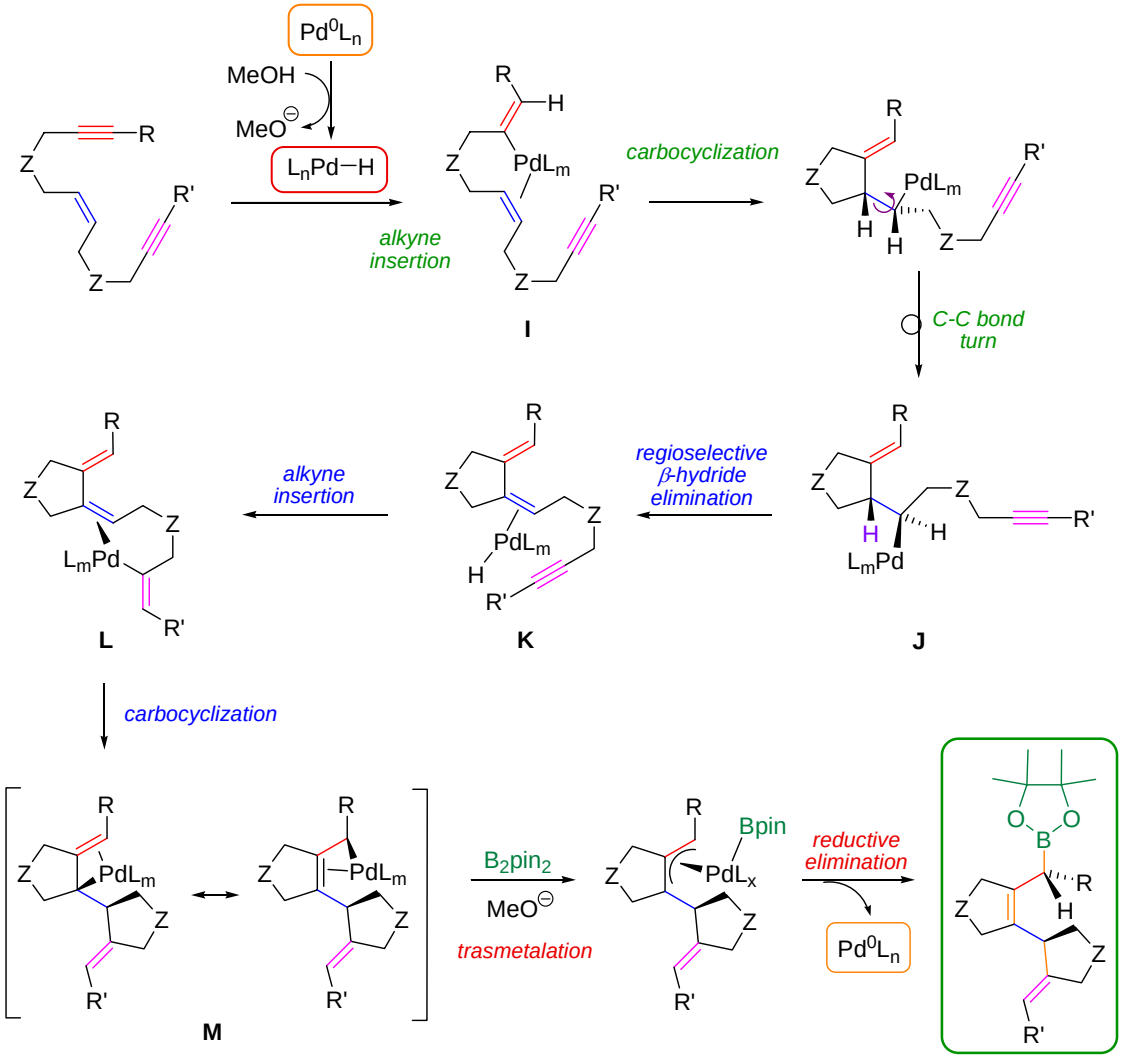


Figure 9. *X-ray diffraction structures from some tricycles.*

[224] Shibata, T.; Kurokawa, H.; Kanda, K. *J. Org. Chem.* **2007,** *72,* 6521-6525.

Regarding to the mechanistic pathway, the reaction probably takes place by formation of a Pd-hydride complex which promotes hydropalladation of the terminal alkyne. After 1,2-insertion of the alkene into alkenyl-Pd intermediate **I** a regioselective *β*-hydrogen elimination from **J** would afford 1,3-diene **K** (*Scheme 27*).

Although related intermediates involved in the Oppolzer reaction usually evolve through elimination of the exocyclic H atoms,[252] the stereospecificity of the overall process suggests the opposite regioselectivity in this case, since a *β*-hydrogen elimination involving the exocyclic chain would destroy the stereochemical information contained in the starting alkene.



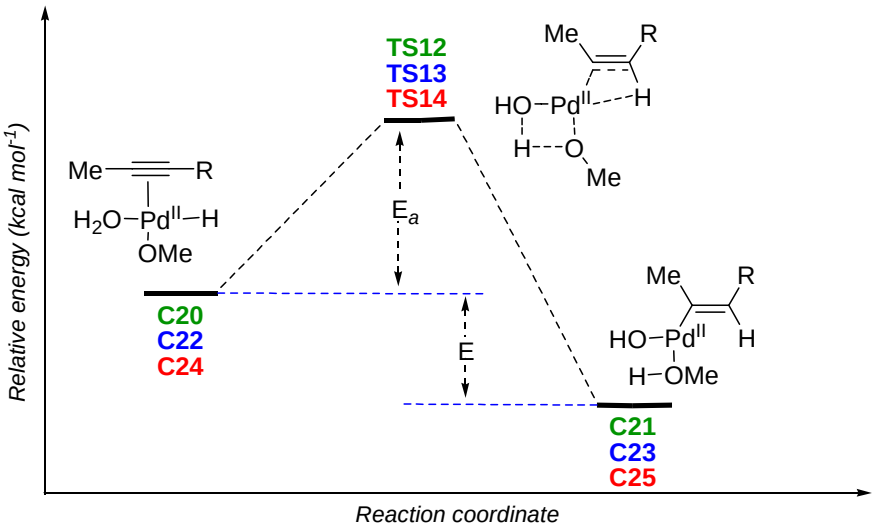
***Scheme 27**. Proposed mechanistic pathway.*

[252] Reviews: (a) Oppolzer, W. *Comprehensive Organometallic Chemistry II*; Abel, E. W.; Stone, F. G.; Wilkinson, G.; Hegedus, L., Eds.; Pergamon Elsevier: Oxford, 1995; Vol. 12, Chapter 8.3. (b) Oppolzer, W. *Angew. Chem., Int. Ed.* **1989**, *28*, 38-52.

Later, insertion of the other alkyne into the Pd–H bond in **K** to give **L** stereoselectively, followed by carbometalation of the diene would give rise to allyl-Pd intermediate **M**. This 1,2-insertion explains the relative stereochemistry observed in the final products. Thus, becoming evident that the stereochemical information contained in the starting double bond travels along the multistep reaction pathway leading to the stereospecific formation of two asymmetric centers.

Finally, methoxide-promoted transmetalation of **M** with the boron reagent and reductive elimination would lead to the observed final products.

In order to confirm the regioselectivity of the process, which would explain the different behaviour of the terminal and internal alkynes on the insertion in the Pd–H bond, some computational data were obtained using Gaussian 03 at DFT level (see *Appendix I: Computational Section*). Thereby, calculations shown that in the case of terminal alkynes (R = H, **C20-TS12-C21**, E_a = 7.8 kcal mol^{-1}, E = -10.7 kcal mol^{-1}) the reaction proceeded through a lower activation energy pathway than internal derivatives (R = Me, E_a = 9.6 kcal mol^{-1}, E = -5.5 kcal mol^{-1}; R = Ph, E_a = 8.8 kcal mol^{-1}, E = -6.0 kcal mol^{-1}), and the process were also more exotermic (*Scheme 28*). Therefore, these energy values, agreed with the experiments obtained from asymmetrical substrates, supported the results where terminal alkynes seemed to be always more reactive (see *Table 7*).



C20-TS12-C21 : R = H { E_a = 7.8 kcal mol^{-1} ; E = -10.7 kcal mol^{-1}

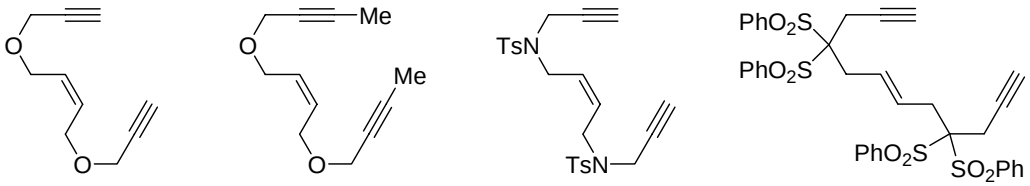
C22-TS13-C23 : R = Me { E_a = 9.6 kcal mol^{-1} ; E = -5.5 kcal mol^{-1}

C24-TS14-C25 : R = Ph { E_a = 8.8 kcal mol^{-1} ; E = -6.0 kcal mol^{-1}

Scheme 28. *Alkyne insertion. B3LYP/6-31G(d) (C, H, O), LANL2DZ (Pd); Δ(E+ZPE) is given in kcal mol^{-1} (gas-phase).*

Moreover, comparing the energy values of the internal alkynes, the phenyl derivative (**C22-TS13-C23**, E_a = 8.8 kcal mol^{-1}, E = -6.0 kcal mol^{-1}) was slighty more reactive than methyl derivative (**C24-TS14-C25**, E_a = 9.6 kcal mol^{-1}, E = -5.5 kcal mol^{-1}) (*Scheme 28*). This is also consistent with the mixture of regioisomers (60:40, **26g**) obtained by the reaction with assymetrical enediyne **(*Z*)-25g**. The structure of the major regioisomer of the resulting mixture can be explained starting from phenyl acetylene moiety preferently.

Unlike the case of enyne borylative cyclization, where many types of groups were allowed at the atom-bridge position, for these enediynes the malonate derivatives seem to be necessary at the tether of the structure. Despite related substrates containing other tether groups, such as O (both terminal or internal alkynes, *Z*-alkene, **30** and **31**), NTs (terminal alkynes, *Z*-alkene, **32**), or bis(sulfonyl)metane (terminal alkynes, *E*-alkene, **33**) were prepared and under the optimized conditions, none of them afforded the desired allylboronates (*Figure 10*). Probably, like in the case of enynes, a weaker Ingold-Thorpe effect was operating for each cyclization and the intermediate *β*-hydride elimination step was not conformationally favoured.

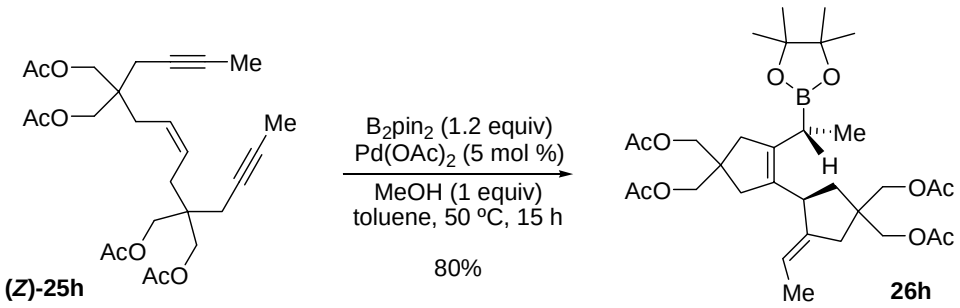


30 **31** **32** **33**

***Figure 10**. Other tethered 6-ene-1,11-diynes.*

However, the tetraacetate derivative **(Z)-25h** obtained from reduction of **(Z)-25b** did undergo the transformation with good yield (80%) leading to the allylboronate **26h** (*Scheme 29*).

[246] (a) Beesley, R. M.; Ingold, C. K.; Thorpe, J. F. *J. Chem. Soc., Trans.* **1915**, *107*, 1080-1106. (b) Jung, M.; Piizzi, G. *Chem. Rev.* **2005**, *105*, 1735-1766.



Scheme 29. *Synthesis of allylboronate* ***26h***.

In addition to the enediynes described before, other substrates such as **34** and **35** were prepared but the reaction did not take place (*Figure 11*). In particular, compound **34** was designed in order to prevent the *β*-elimination of the endocyclic hydrogen which could give rise the the direct second cyclization affording alkenylboronates, but the reaction led to a mixture of nonseparable cyclized compounds. With substrate **35** the goal was to obtain the analogous six-membered rings allylboronate following the same approach that with 1,7-enyne **7**, however, under reaction conditions the starting enediyne was almost totally recovered.

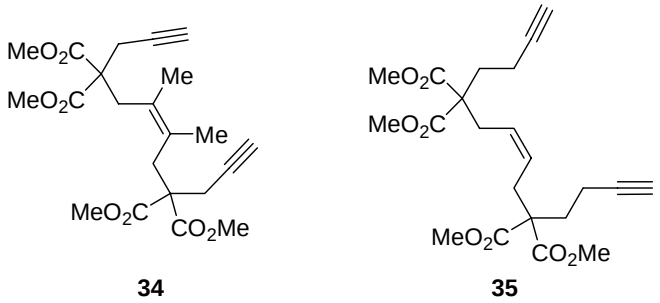


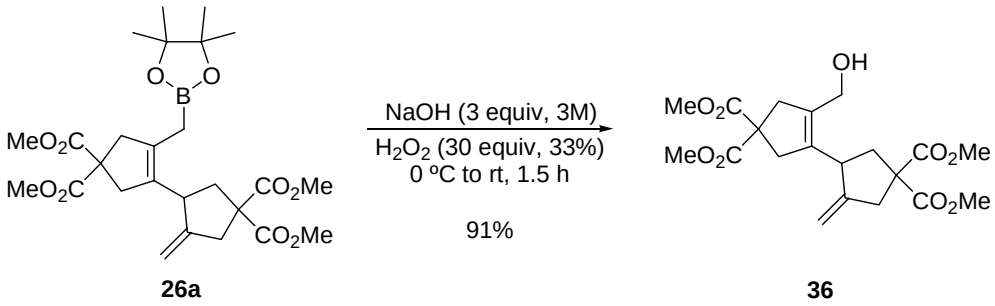
Figure 11. *Other failed subtrates.*

In order to take advantage of the synthetic possibilities provided from these new allylboronates and enhance the importance of the borylative bicyclization, some functionalization methods, such as oxidation to alcohols or C–C bond forming reactions (allylation and Suzuki coupling), were approached.

First of all, oxidation process was performed under the same conditions optimized in the case of alkylboronates. Thereby, allylboronate **26a** was reacted under alkaline aqueous conditions[91b] in the presence of a large excess of oxygen peroxyde (33% w/v). Thus, the

[91] (b) Snyder, H. R.; Kuck, J. A.; Johnson, J. R. *J. Am. Chem. Soc.* **1938**, *60*, 105-111.

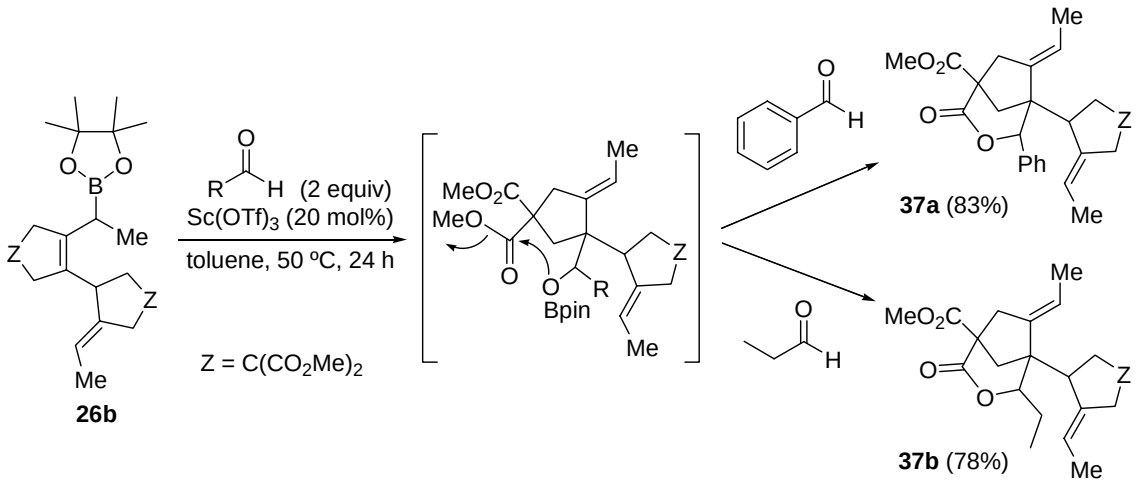
corresponding allylalcohol **36**, was obtained in high yield (91%) easily isolated by sylica gel column chromatography (*Scheme 30*).



Scheme 30. *Formation of allylalcohols from allylboronates.*

As previously mentioned in the introduction, allylboronates have gained a prominent position as a useful class of synthetic intermediates, mainly due to the employ of these reagents in the stereoselective synthesis of homoallylic secondary alcohols by an allyl transfer reaction to aldehydes. Specifically, the addition of Lewis[,] and Brönsted acids as catalysts of the reaction has been developed in the last years.

That was the reason to approach this interesting synthetic method with the bicyclic allylboronates. By this way, when allylboronate **26b** was reacted with aldehydes, in the presence of a Lewis acid such as $Sc(OTf)_3$ in toluene, the lactones **37** were prepared in good yields (*Scheme 31*). Other Lewis acids such as $BF_3{\cdot}Et_2O$ or $Y(OTf)_3$ were also tested leading to lower yields.



Scheme 31. *Synthesis of lactones from allylation of aldehydes.*

[122] (a) Hall, D. G. *Synlett* **2007**, 1644-1655. (b) Carosi, L.; Lachance, H.; Hall, D. G. *Tetrahedron* **2005**, *46*, 8981-8985.
[124] Rauniyar, V.; Hall, D. G. *J. Am. Chem. Soc.* **2004**, *126*, 4518-4519.
[127] (a) Elford, T. G.; Arimura, Y.; Yu, S. H.; Hall, D. G. *J. Org. Chem.* **2007**, *72*, 1276-1284. (b) Rauniyar, V.; Zhai, H.; Hall, D. G. *J. Am. Chem. Soc.* **2008**, *130*, 8481-8490.

The reaction pathway involves the addition of the allylboronate to the aldehyde catalyzed by the Lewis acid likely to form an hydroxy-ester intermediate (*Scheme 31*). This intermediate could not be isolated and finally cyclized in the reaction mixture leading to the lactone.[a,253] Moreover, the resulting lactones could subsequently be transformed into useful synthetic intermediates such it has been already reported in the literature.[b]

Once again, suitable crystals of the lactone **37a** could be obtained for X-ray diffraction analysis (*Figure 12*).

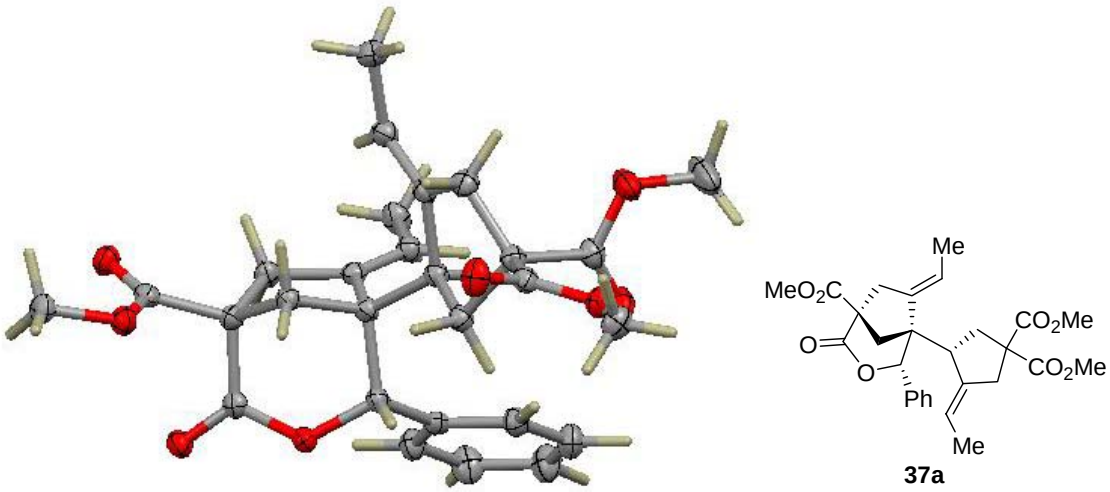


***Figure 12**. X-ray diffraction structure from lactone **37a**.*

On the other hand, although Suzuki coupling were described with allylboronates,[254] the coupling was not achieved under reported conditions. Therefore, following the same approximation that was employed in the case of alkylboronates, the transformation of the allylboronates into the correspondent trifluoroborate salts was attempted.[35a,b] Thereby, allylboronates **26a** and **26b** were subjected to the trifluoroborate salt formation conditions in the presence of a saturated aqueous solution of KHF_2 in acetonitrile at rt.[33] Unexpectedly, the boronic acids **38** were obtained (confirmed by NMR and HRMS

[33] (a) Vedejs, E.; Chapman, R. W.; Fields, S. C.; Lin, S.; Schrimpf, M. R. *J. Org. Chem.* **1995**, *60*, 3020-3027. (b) Vedejs, E.; Fields, S. C.; Hayashi, R.; Hitchcock, S. R.; Powell, D. R.; Schrimpf, M. R. *J. Am. Chem. Soc.* **1999**, *121*, 2460-2470.

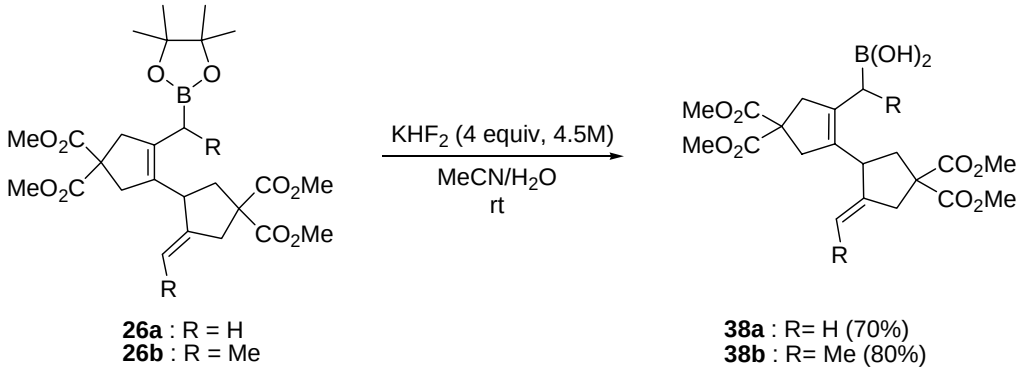
[35] (a) Molander, G. A.; Ellis, N. *Acc. Chem. Res.* **2007,** *40*, 275-286. (b) Doucet, H. *Eur. J. Org. Chem.* **2008**, 2013-2030.

[123] (a) Kennedy, J. W. J.; Hall, D. G. *Angew. Chem., Int. Ed.* **2003**, *42*, 4732-4739. (b) Kennedy, J. W. J.; Hall, D. G. *J. Org. Chem.* **2004**, *69*, 4412-4428.

[253] Kennedy, J. W. J.; Hall, D. G. *J. Am. Chem. Soc.* **2002**, *124*, 898–899.

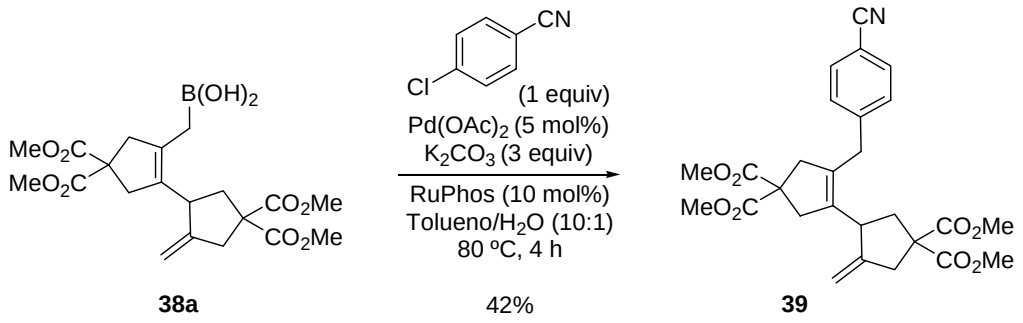
[254] (a) Kotha, S.; Behera, M.; Shah, V. R. *Synlett* **2005**, 1877-1880. (b) Kotha, S.; Shah, V. R.; Mandal, K. *Adv. Synth. Catal.* **2007,** *349*, 1159-1172.

experiments) as sticky white oils after sucessive washes with diethyl ether, and finally as sticky white solids in good yields (calculated by NMR, *Scheme 32*).



Scheme 32. *Preparation of allylboronic acids* ***38***.

By using these boronic acids as Suzuki partners, reaction of **38a** under optimized conditions with electron-withdrawing derivative *p*-chlorobenzonitrile allowed the synthesis of the desired coupled product **39** in a moderate yield (42%). However, the analogous more hindered secondary allylboron derivative **38b** did not undergo the reaction in the same coupling conditions (*Scheme 33*).



Scheme 33. *Suzuki couping of allylboronic acid* ***38a***.

In summary, a tandem borylative dicyclization reaction in which two C–C and one C–B bonds are formed stereospecifically in smooth conditions has been developed to afford allylboronates. The stereochemical outcome depends on the starting alkene configuration and this information travels along the multistep reaction pathway leading to the stereospecific formation of two new assymetric centers. Moreover, the isolation

[111] Dreher, S. D.; Lim, S.-E.; Sandrock, D. L.; Molander, G. A. *J. Org. Chem.* **2009**, *74*, 3626-3631.

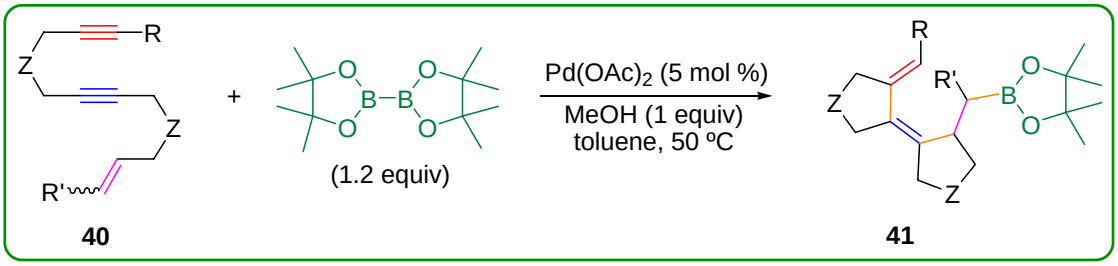
of intermediates 1,3-dienes suggests a regioselective *β*-hydrogen elimination along the reaction pathway. Finally, some transformations of these derivatives has been achieved such allowing the preparation of alcohols, allylborations and Suzuki couplings to give rise new C–C bonds.

2.2 Pd-Catalyzed Borylative Bicyclization of 1-Ene-6,11-diynes to Alkylboronates

In order to extend the borylative polycylization process to other substrates and with the initial aim of trapping the Pd-intermediates formed along the reaction pathway, the possibility of changing the positions of the insaturated moieties in the molecule was considered.

Thereby, by exchanging one of the alkyne moieties and the corresponding alkene, the previously studied endiynes turn into 1-ene-6,11-diynes. The structure of this molecule can be considered a chimera containing a diyne and an enyne which share a triple bond.

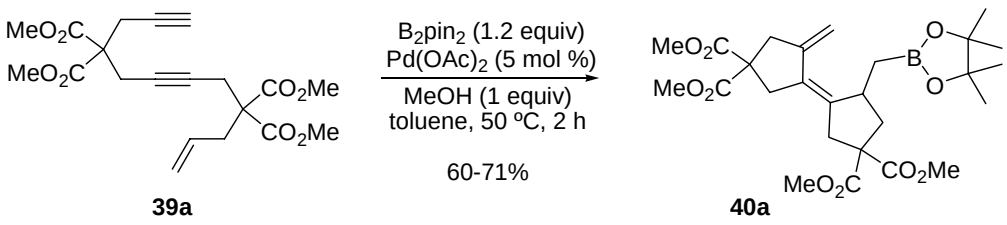
When 1-ene-6,11-diynes **40** were reacted under the borylative polycyclization conditions the following bicyclic alkylboronates **41** were obtained (*Scheme 34*).



Scheme 34. *Pd-catalyzed bicyclization/borylation of 1-ene-6,11-diynes.*

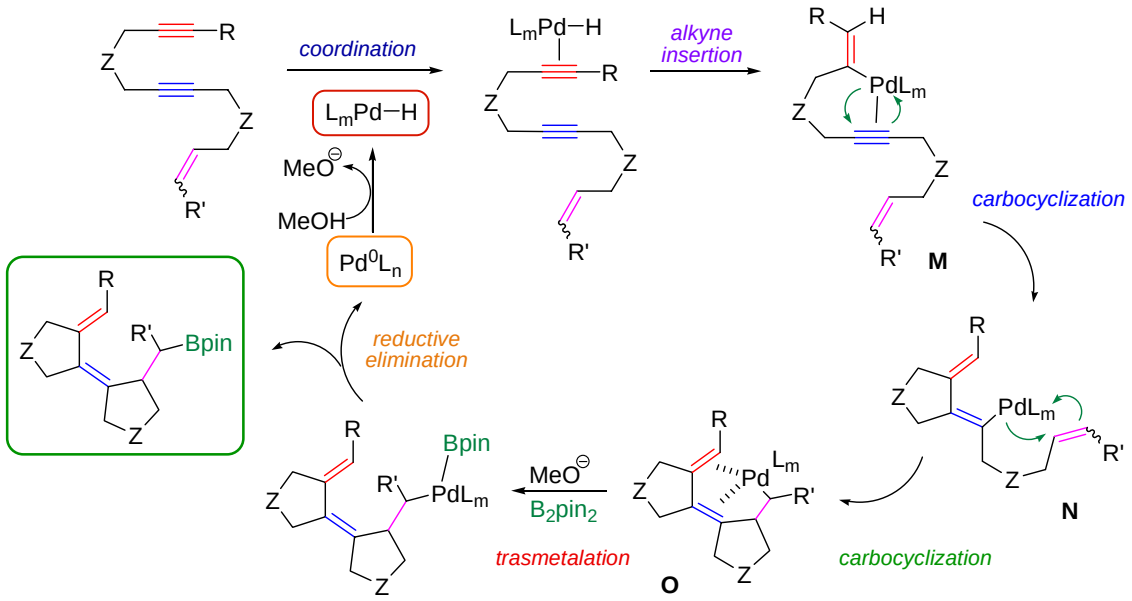
This cascade reaction provided two C–C and one C–B bond and two new stereogenic centers in a single stereoselective process.

The first experiment was carried out with simple bis(malonate)-tethered enediyne **40a** and afforded the corresponding bicyclic alkylboronate **41a** in moderate to good yield (60-71% depending upon the scale, *Scheme 35*).



Scheme 35. *Pd-catalyzed bicyclization/borylation of 1-ene-6,11-diyne* ***39a***.

This result allowed to confirm the expected mechanistic pathway, the cascade process seems to take place with no intervention of *β*-hydrogen elimination steps, and probably the alkenyl-Pd intermediate is trapped directly by the pendant alkene moiety (*Scheme 36*).



***Scheme 36**. Proposed mechanistic pathway.*

Thus, the reaction probably takes place by formation of a Pd-hydride complex which is originated, preferently, from the hydropalladation of the terminal alkyne rather than of the internal linker triple bond. Next, 1,2-insertion of the linker triple bond into the alkenyl-Pd intermediate **N** would afford the first cyclization and a new alkenyl-Pd intermediate **O**. Then, this intermediate **O** would be directly trapped by the pendant double bond giving rise to an alkyl-Pd intermediate **P** (*Scheme 36*). And finally, methoxyde-promoted transmetallation with the bis(pinacolato)diboron and subsequent reductive elimination would lead to the final alkylboronate.

It is worthwhile to note that, regardless the presence of *β*-hydrogens susceptible to be eliminated in the alkyl-Pd intermediate **P**, some stabilization due the coordination of the Pd from the diene moiety seems to be taking place. Therefore, transmetalation process is faster than possible *β*-hydrogen elimination. In fact, *β*-elimination products have been rarely detected and isolated.

With the aim of explore the scope of the process, the reaction was extended to a large number of related substrates including several modifications at the different moieties of

the enediyne. Those modifications were related with the following aspects of the initial substrate:

- The substitution on the alkene: monosubstituted, 1,1- and 1,2-disubstituted (*Z*/*E* geometry with coordinating groups: allylic esters and ethers, or non-coordinating groups) and trisubstituted alkenes.

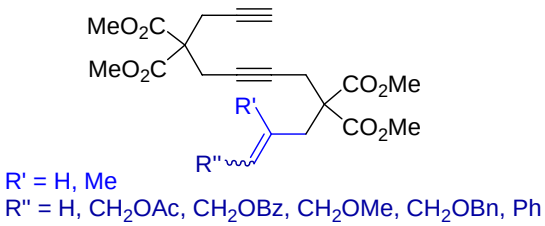


Figure 13. *Substitution on the double bond.*

- The nature and substitution on the atom-bridge moiety: ether, amide, methylene, malonate (dimethyl) or bis(sulfonyl)methane.

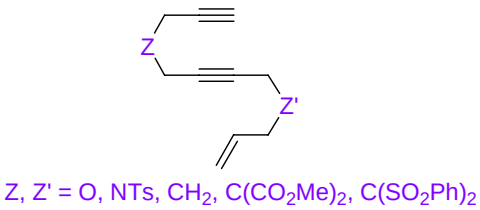


Figure 14. *Substitution on the tethers.*

- Triple bond nature: terminal and internal alkynes.

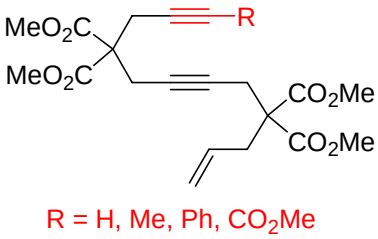


Figure 15. *Substitution on the external triple bond.*

As shown before, when both atom-bridge moieties were malonate derivatives (**40a**) the reaction worked with good yield (**41a**, 60-71%, *Scheme 35*). By this reason, substrates of this kind with susbtitution on the alkene were prepared. When substituted enediynes **40b-e** were reacted under optimized borylative polycyclization conditions the corresponding alkylboronates **41b-e** were obtained in good yields (*Table 8*).

In the case of allylic ester susbtitution (entries 1 and 2) the yields were similar to the case of **41a**, despite a possible additional stabilization due the presence of a coordinating group in the allylic position.

On the other hand, with enediynes **40d** and **40e**, in which a potential *β*-hydrogen elimination was blocked by the presence of a methyl group, both alkylboronates (**41d** and **41e**) were afforded in the highest yields (81% and 80%, respectively). Moreover, although enediyne **40e** is similar to 1,6-enyne **11** (taking account the substitution on the alkene moiety), cyclopropyl derivatives were not obtained in this case probably due to the more hindered exocyclic doble bond, which precludes the reinsertion of the alkyl-Pd intermediate into that alkene.

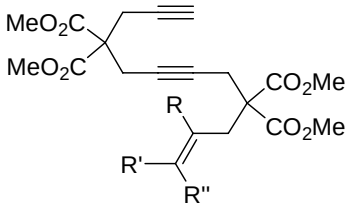
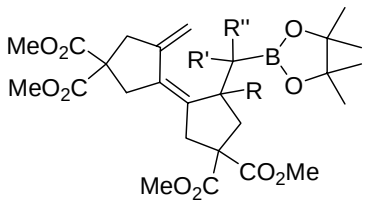
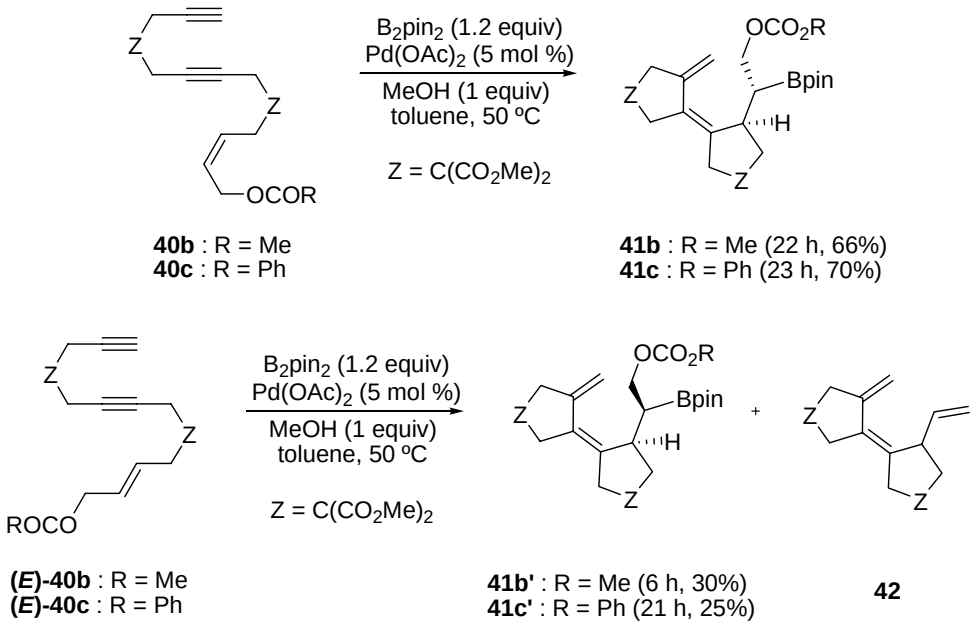
	substrate	time (h)	product	yield (%)
				
1	**40b**	22	**41b :** R = H, R' = H, R'' = CH_2OAc	66
2	**40c**	23	**41c :** R = H, R' = H, R'' = CH_2OBz	70
3	**40d**	4	**41d :** R = Me, R' = H, R'' = H	81
4	**40e**	3.5	**41e :** R = Me, R' = Ph, R'' = H	80

***Table 8**. Alkylboronates from subtituted double bond derivatives.*

With the aim of study the stereoespecificity of the process, the *E* isomers of **40b** and **40c** were prepared. Thus, when the reaction was carried out with **(*E*)-40b** and **(*E*)-40c** the corresponding diastereomers of **41b** and **41c** were obtained (**41b'** and **41c'**), respectively (*Scheme 37*). The isolation of these diastereomers was difficult due to the

more feasible *β*-oxygen elimination process leading to low yields along with triene bicyclic product (**42**).



***Scheme 37**. Relative stereochemistry and demostration of the stereoespecificity.*

The relative stereochemistry of the new stereogenic centers was determined by the similarity of the second cyclization process from intermediate **N** (*Scheme 36*) with the cyclization of 1,6-enynes (*Scheme 7*).

Unfortunately, when analogous allylic ethers (**43** and **44**, *Figure 16*) were reacted under the cyclization conditions only mixtures of *β*-elimination products were obtained.

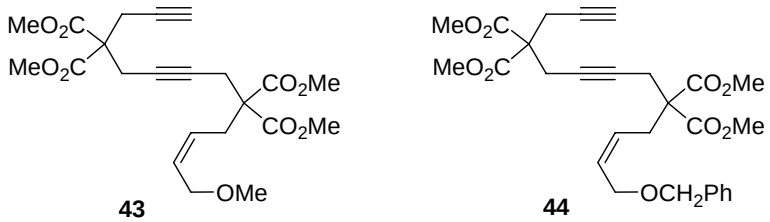
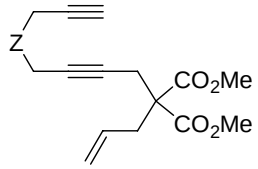
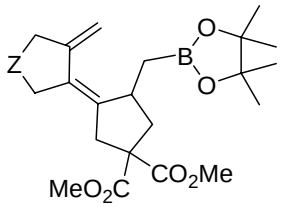


***Figure 16**. Analogous allylic ether derivatives.*

In order to analyze the effect produced by the combination of two different tethers on the reaction outcome several substrates were tested. Thus, the following compounds, in which diyne moiety contains a non-malonate tether, were prepared (**40f-h**) and reacted

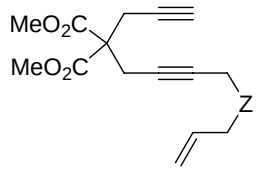
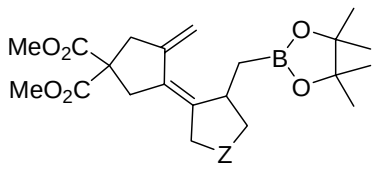
under the cyclization conditions leading to the corresponding alkylboronates (**41f-h**) in moderate to low yields (*Table 9*).

	substrate	time (h)	product	yield (%)
				
1	**40f**	18	**41f :** Z = NTs	44
2	**40g**	22	**41g :** Z = O	14
3	**40h**	5	**41h :** Z = CH_2	30[a]

[a] Calculated NMR yield.

Table 9. *Alkylboronates from non-malonate tethered diyne moiety derivatives.*

However, the enediynes containing the non-malonate tether at the enyne moiety (**40i-l**) were reacted under cyclization conditions leading to higher yields in all the cases (**41i-l**) (*Table 10*).

	substrate	time (h)	product	yield (%)
				
1	**40i**	15	**41i :** Z = NTs	51
2	**40j**	14.5	**41j :** Z = O	41
3	**40k**	3.5	**41k :** Z = CH_2	64[a]
4	**40l**	24	**41l :** Z = $C(SO_2Ph)_2$	54

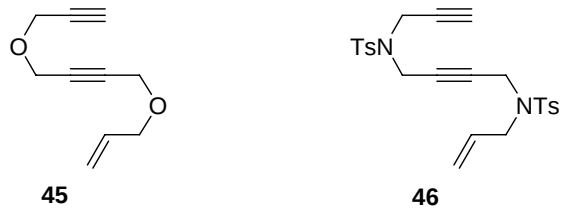
[a] Calculated NMR yield.

Table 10. *Alkylboronates from non-malonate tethered enyne moiety derivatives.*

These results pointed that the limiting step during the reaction course was the first cyclization, that is, the cyclization in which the diyne was involved. Therefore, when the cyclization of the diyne moiety was facilitated, the second one was quickly completed. Whereas when the first cyclization failed or was disfavoured, the second one did not take place or it was so slowly that led to low yields, as a result of the easy decomposition of the Pd-intermediates.

The results of both tables (*Table 9 and 10*) were consistent with those obtained before in the borylative cyclization of enynes where non-malonate tethers led to lower yields. Probably, as in the case of simple enynes, a weaker Ingold-Thorpe effect was operating for the cyclization that involved the non-malonate tether moiety.

Moreover, other subtrates such as diether **45** and diamide **46** were tested under the reaction conditions with no success (*Figure 17*). One explanation, as in the case of 6-en-1,11-diynes with two non-malonate tethers, a weaker Ingold-Thorpe effect, due the more flexibility of the whole molecule, operated in each cyclization precluding, in this way, the reaction.

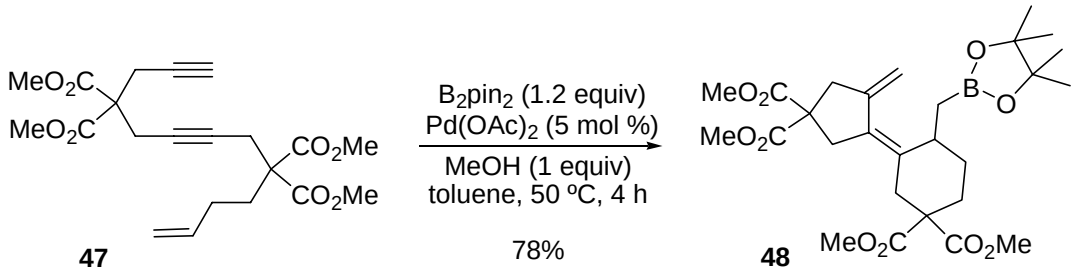


45 **46**

Figure 17*. Other failed substrates.*

Taking advantage of the high capability of cyclization of the enyne moiety containing the malonate moiety, the enediyne **47**, related to the 1,7-enyne **5**, was prepared. The reaction led to the bicyclic compound with a five and a six-membered ring (**48**) in high yield (78%) (*Scheme 38*).

[246] (a) Beesley, R. M.; Ingold, C. K.; Thorpe, J. F. *J. Chem. Soc., Trans.* **1915**, *107*, 1080-1106. (b) Jung, M.; Piizzi, G. *Chem. Rev.* **2005**, *105*, 1735-1766.



Scheme 38. *Synthesis of bicyclic five and six-membered rings alkylboronate.*

Once again, suitable crystals for X-ray diffraction from alkylboronate **48** were obtained. The structure clearly shown the double bond connecting five and six-membered rings (*Figure 18*).

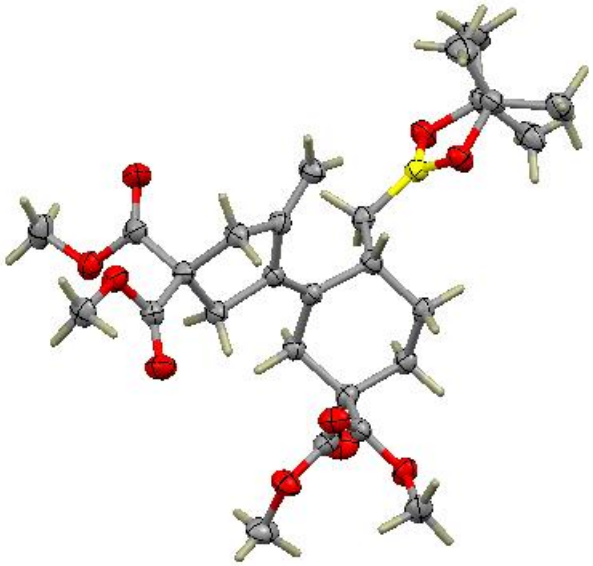
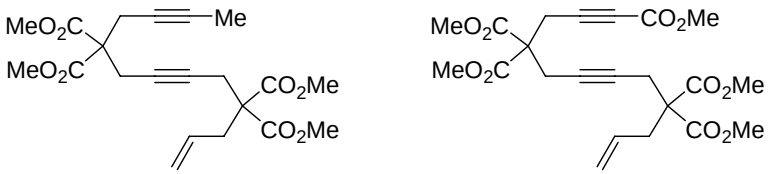


Figure 18. *X-ray diffraction structure from alkylboronate* ***48***.

The substitution on the external alkyne provided a third variety of suitable substrates to be tested under polycyclization conditions. Several enediynes of this type were prepared and all the cases afforded mixtures of nonseparable products. The explanation of this fact could be the potential competitivity between the two alkynes against the insertion in the Pd-hydride species. Whereas in the case of one terminal and the linker alkyne the insertion took place regioselectively at the terminal triple bond, in this case both moieties are internal alkynes that compete leading to final products through different processes.

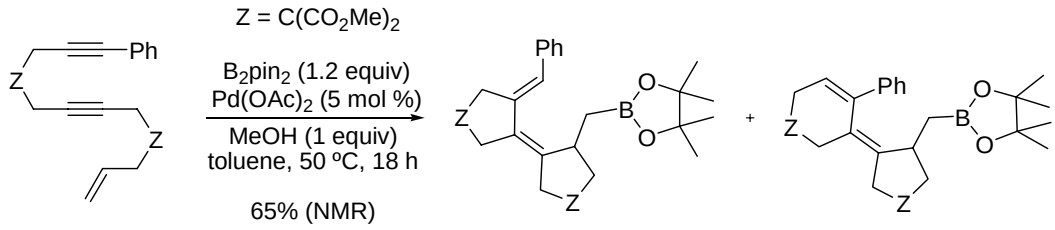
For instance, internal enediyne **49** (*Figure 19*) gave a mixture of the expected alkylboronate with other non identified products. Probably, one of them could be the alkylboronate resulting from the cyclization of the enyne moiety leaving the pendant alkyne without any reaction. For the more reactive acetylene ester **50** (*Figure 19*), corresponding alkylboronate was obtained as a mixture probably with tricyclic products without any incorporation of Bpin (determined by NMR and HPLC/ESI experiments).



49 **50**

***Figure 19**. Internal enediynes.*

However, one of the internal enediynes prepared afforded a mixture of two compounds that could be partially isolated (*Scheme 39*). Thus, phenyl derivative **51** reacted under cyclization conditions supplying two different alkylboronates in an almost equitative ratio (**52**:**53**, 60:40) with 65% yield of the mixture (calculated by NMR) and 12% isolated yield for each compound. One of them was identified as the expected alkylboronate **52** and the other resulted to be an isomer with a six-membered ring (**53**).

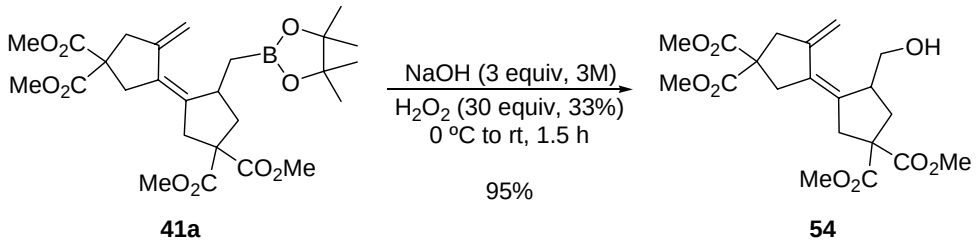


51 **52** (12%) **53** (12%)

***Scheme 39**. Synthesis of two isomers from an internal enediyne.*

Once more, with the aim of taking advantage of the synthetic possibilities provided from these new bicyclic alkylboronates and enhancing the importance of the borylative bicyclization, some functionalization methods such as oxidation to alcohols or C–C bond forming reactions by Sukuki coupling were approached.

First of all, oxidation process was carried out under the same conditions optimized in the case of alkylboronates derived from enynes. Thereby, alkylboronate **41a** was transformed under alkaline aqueous conditions[91b] in the presence of a large excess of oxygen peroxyde (33% w/v). Thus, the corresponding primary alcohol **54** was achieved in high yield (95%) after an easy purification by sylica gel column chromatography (*Scheme 40*).



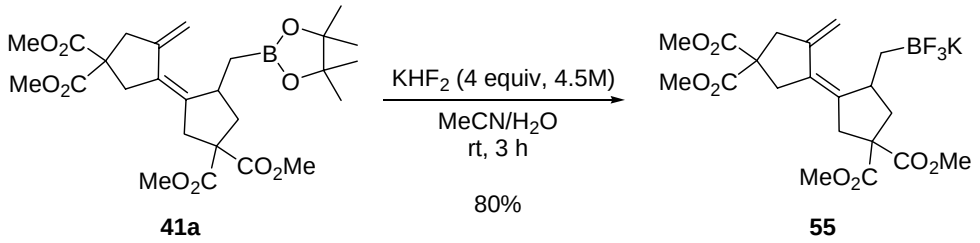
41a **54**

Scheme 40. *Formation of alcohols from bicyclic alkylboronates.*

Furthermore, although several Suzuki coupling conditions were tested with alkylboronates, the coupling was not achieved since the use of C(sp^3)–B bonds in this type of coupling is still challenging.[108] Therefore, as previously mentioned, other efficient approximation to this objetive could be the transformation of the alkylboronates into the corresponding trifluoroborate salts.[35a,b] These salts have been demostrated to be valuable partners in Suzuki coupling with a large number of electrophiles, regarless to the hybridation of the carbon involved in the reaction.

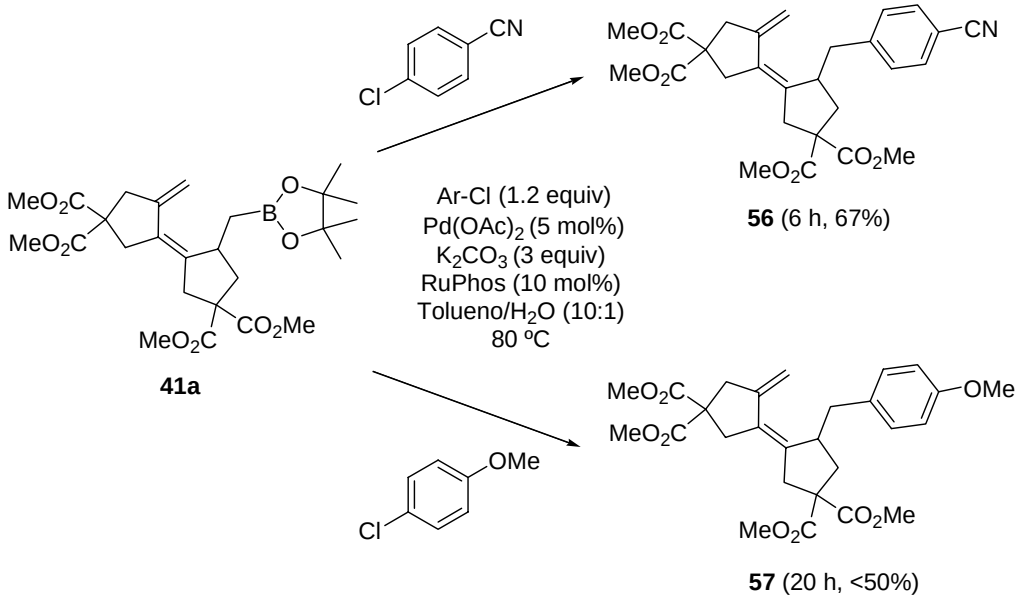
Thereby, alkylboronate **41a** was transformed into the trifluoroborate salt in the presence of a saturated aqueous solution of KHF_2 in acetonitrile at rt. The borate salt **55** was obtained as a white solid in good yield (80%) after sucessive washes with diethyl ether (*Scheme 41*).

[35] (a) Molander, G. A.; Ellis, N. *Acc. Chem. Res.* **2007,** *40*, 275-286. (b) Doucet, H. *Eur. J. Org. Chem.* **2008**, 2013-2030.
[91] (b) Snyder, H. R.; Kuck, J. A.; Johnson, J. R. *J. Am. Chem. Soc.* **1938**, *60*, 105-111.
[108] Chemler, S. R.; Trauner, D.; Danishefsky, S. J. *Angew. Chem., Int. Ed.* **2001**, *40*, 4544-4568.



Scheme 41. *Formation of bicyclic alkytrifluoroborate salts.*

According to previous reported conditions for the Suzuki coupling,[111] trifluoroborate salt **55** was coupled with aryl chorides, either with electron-withdrawing or electron-donor derivatives such as *p*-chlorobenzonitrile and *p*-chloroanisol, respectively. Thus, the coupled products (**56** and **57**) were obtained with moderate to good yields (*Scheme 42*). In particular, by using the electrophile *p*-chlorobenzonitrile, the coupled product **56** was achieved with 67% yield after 6 h under the optimized conditions already employed in the case of monocyclic trifluoroborate salts. However, under similar conditions, the reaction with electron-donor *p*-chloroanisol afforded the corresponding coupled product **57** in a lower yield (<50%) with a small amount of a nonseparable impurity.[111]



Scheme 42. *Suzuki coupling of bicyclic alkyltrifluoroborate salts.*

[111] Dreher, S. D.; Lim, S.-E.; Sandrock, D. L.; Molander, G. A. *J. Org. Chem.* **2009**, *74*, 3626-3631.

In conclusion, a cascade borylative bicyclization process for a widely scoped stereoselective synthesis of bicyclic homoallylic alkylboronates has been developed under smooth conditions. Two new bonds, one C–C and one C–B, are formed and even two new asymmetric centers can be stereospecifically obtained. It tolerates the presence of *β*-hydrogens and avoids the use of highly nocleophilic reagents being compatible with a wide variety of functional groups. Moreover, some functionalizations of these derivatives have been carried out such as the transformation into alcohols, or the synthesis of alkyltrifluoroborate salts and C–C coupling products by Suzuki reaction.

3. Pd-Catalyzed Borylative Cyclization of Allenynes and Enallenes

One of the objectives of our research was the extension of the new borylative cyclization to other substrates such as dienes and diynes. However, the reaction of these compounds was no successful (*Figure 20*). Thus, when diallylmalonate **58** was reacted under optimized conditions the diene was almost totally recovered, even when higher temperatures were used showing the low reactivity of the double bond to initiate the process. In contrast, a high reactivity was observed with either symmetrical or nonsymmetrical diynes **59**. They reacted so fast, even at low temperatures, that afforded dark reaction crudes in which the starting sustrate seemed to be polymerized.

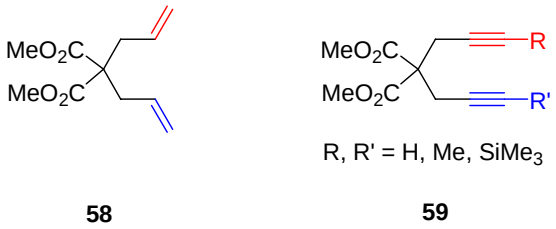
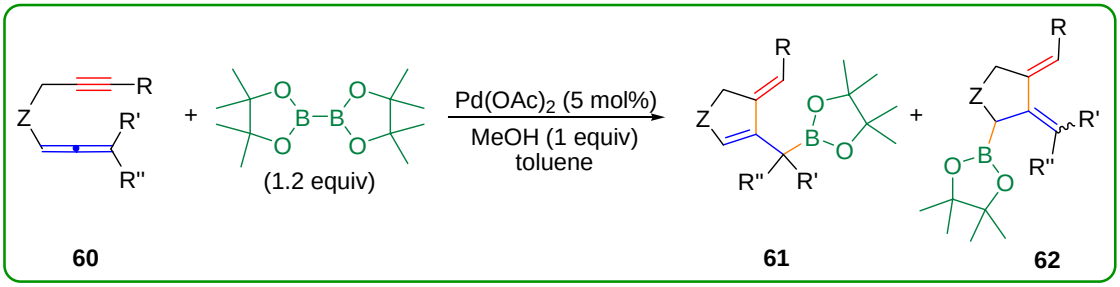


Figure 20. *Dienes and diynes tested.*

As a result of the observed behaviour of those compounds, other kinf of insaturated moieties showing a different reactivity was considered. By this way, the preparation of allenynes and later of enallenes was approached in order to explore its reactivity on the borylative cyclization reaction.

Thereby, when 1,5-allenyne **60** was subjected to reaction with bis(pinacolato)diboron in the presence of $Pd(OAc)_2$ and MeOH in toluene, a mixture of two five-membered ring allylboronates, **61** and **62,** was formed (*Scheme 43*).[255]



Scheme 43. *Pd-catalyzed cyclization/borylation of 1,5-allenynes.*

[255] Pardo-Rodríguez, V.; Marco-Martínez, J.; Buñuel, E.; Cárdenas, D. J. *Org. Lett.* **2009**, *11*, 4548-4551.

The formation of these two regioisomers implied a formal 1,7- and 1,5-hydroboration of the 1,5-allenyne, respectively, with concomitant carbocyclization, affording one C–C and one C–B bonds in a single operation.

In order to study the reaction scope, terminal and internal 1,5-allenynes (referred to the alkyne moiety) with variation on the allene substituents were prepared (*Figure 21*).

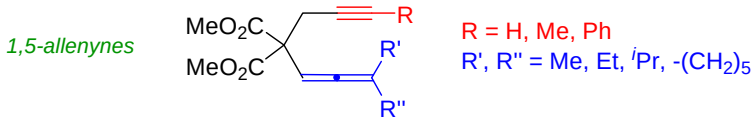
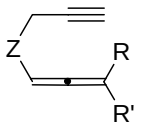
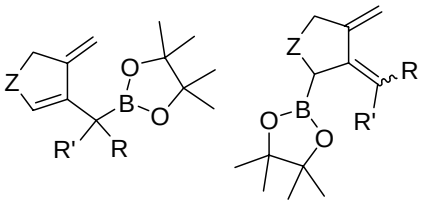


Figure 21. *Possible modifications on the 1,5-allenynes.*

First of all, terminal allenynes **60a-d** afforded the corresponding allylboronates, **61a-d** and **62a-d**, with moderate to good yields (*Table 11*), being the best results those obtained from allenynes **60a** and **60d** (ca. 80% yield).

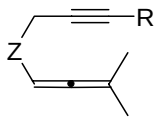
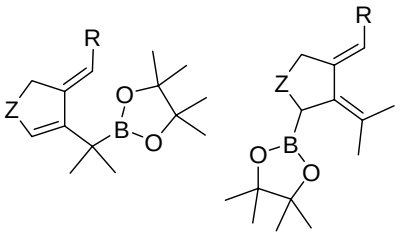
	substrate	T (ºC)	time (h)	yield (%) / ratio[a]
		Z = C(CO2Me)2		
1	**60a :** R = R' = Me	50	4	82[b] / **61a:62a** (97:3)
2	**60b :** R = Me, R' = Et	50	4	67 / **61b:62b** (89:11)
3	**60c :** R = Me, R' = ^{i}Pr	-20	14	60 / **61c:62c** (67:33)
4	**60d :** R = R' = -$(CH_2)_5$	50	4	80 / **61d:62d** (91:9)

[a] Isomers **61** and **62** were were completely separated in most cases.

[b] $Pd(OAc)_2$ (10 mol%) was added.

Table 11. *Allylboronates from terminal 1,5-allenynes.*

However, lower yields were obtained in the case of internal allenynes **60e** and **60f** (*Table 12*).

	substrate	T (ºC)	time (h)	yield (%) / ratio[a]
		Z = $C(CO_2Me)_2$		
1	**60e :** R = Me	50	51	36[b] / **61e:62e** (100:0)
2	**60f :** R = Ph	rt	1.5	42 / **61f:62f** (88:12)

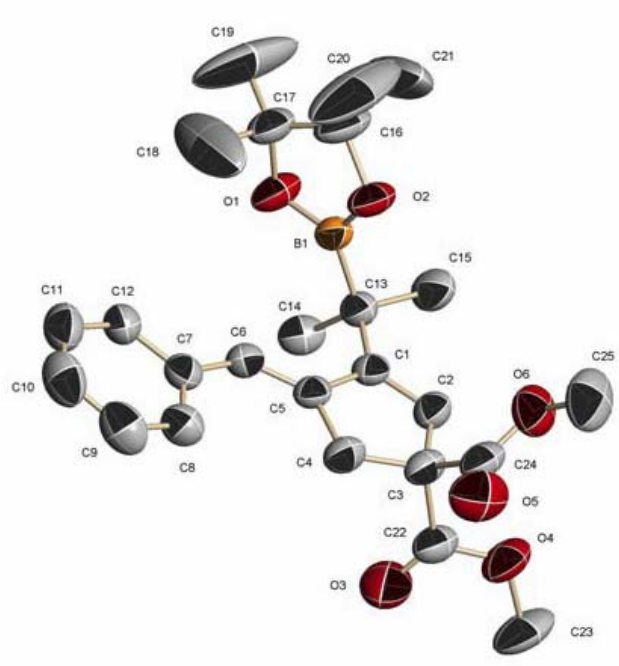
[a] Isomers **61** and **62** were were completely separated in most cases.

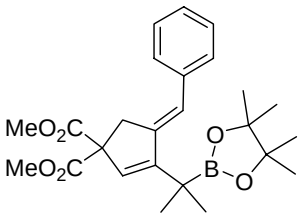
[b] Additional B_2pin_2 (1 equiv) and $Pd(OAc)_2$ (5 mol%) were added after 48 h with no reaction at rt and then heated at 50 ºC.

***Table 12**. Allylboronates from internal1,5-allenynes.*

Probably, the lower reactivity of the internal alkyne with respect to the allene moiety and the potential competition of the allene in the early stages of the reaction pathway could explain those results. Therefore, as will be commented later, internal alkyne and allene moieties compete for the insertion in the Pd-hydride bond.

Moreover, in all cases, both terminal and internal allenyne, the major regioisomer is that in which the boronate is located in the exocyclic position (**61**). One of this major regioisomers (**61f**) afforded suitable crystals for X-ray diffraction analysis (*Figure 22*).





61f

***Figure 22**. X-ray diffraction structure from allylboronate **61f**.*

In contrast, as a result of boronates tend to decomposed in column chromatography when longer retention times are used, minor isomers **62a**, **62b**, **62d**, and **62f** could not be fully characterized due to their instability and fast decomposition in solution.

On the other hand, when the reaction was performed with the 1,6-allenynes (**63**), homologues of **60**, six-membered ring allylboronates **64** and **65** were obtained in formal 1,8- and 1,6-hydroborylative carbocyclizations, respectively (*Scheme 44*).[255]

Scheme 44. *Pd-catalyzed cyclization/borylation of 1,6-allenynes.*

In this case and following the observed results for 1,5-allenynes, only different sustitution on the allene moiety was introduced to study the wideness scope (*Figure 23*).

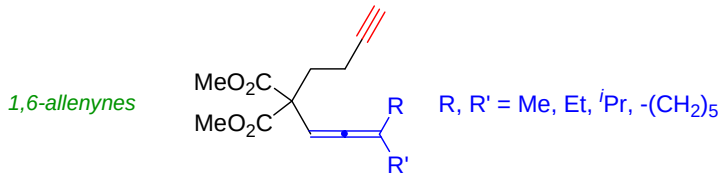
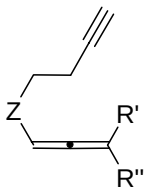
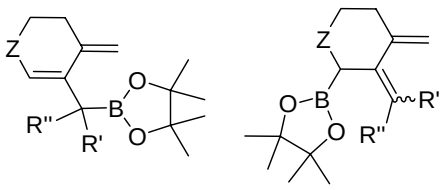


Figure 23. *Modifications on the allene of 1,6-allenynes.*

Reactions of **63a** and **63b** afforded a single regioisomer in each case, **64a** and **64b** respectively, with moderate yields (*Table 13*). However, allenyne **63d** provides an excellent yield (97%), with a significant increase in the endocyclic boronate proportion (**64d**:**65d**, 59:41), and **63c** affords the mixture of allylboronates with the endocyclic boronate as major regioisomer (**65c**). Probably, the steric hidrance exerted by the ^{i}Pr and Cy substituents hampers the transmetalation on the exocylic allylpalladium intermediate, being more favorable on the endocyclic species.

[255] Pardo-Rodríguez, V.; Marco-Martínez, J.; Buñuel, E.; Cárdenas, D. J. *Org. Lett.* **2009**, *11*, 4548-4551.

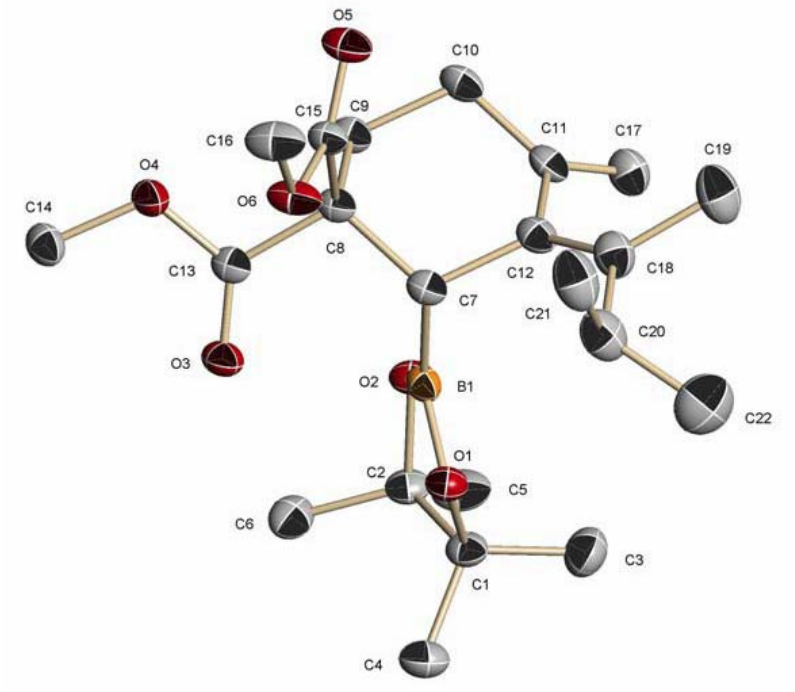
	substrate	T (ºC)	time (h)	yield (%) / ratio[a]
		Z = $C(CO_2Me)_2$		
1	**63a :** R = R' = Me	rt	22	45[b] / **64a:65a** (100:0)
2	**63b :** R = Me, R' = Et	50	4	43 / **64b:65b** (100:0)
3	**63b :** R = Me, R' = Et	rt	3	33 / **64b:65b** (88:12)
4	**63c :** R = Me, R' = ^{i}Pr	rt	24	53 / **64c:65c** (23:77)
5	**63d :** R = R' = -$(CH_2)_5$	rt	1	97 / **64d:65d** (59:41)

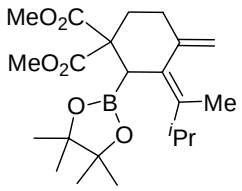
[a] Isomers **60** and **61** were were completely separated in most cases.

[b] A mixture of nonseparable *β*-elimination products was obtained in additional 16% yield.

Table 13. *Allylboronates from terminal 1,6-allenynes.*

Endocyclic allylboronates **65b** and **65c** were obtained as a mixture of geometric isomers. Nevertheless, the X-ray crystal structure of the *E*-isomer of **65c** was determined using a pure sample from a chromatographic partial separation (*Figure 24*).

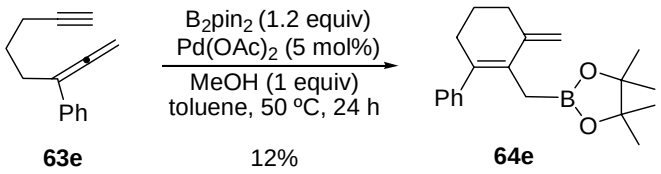




(*E*)-65c

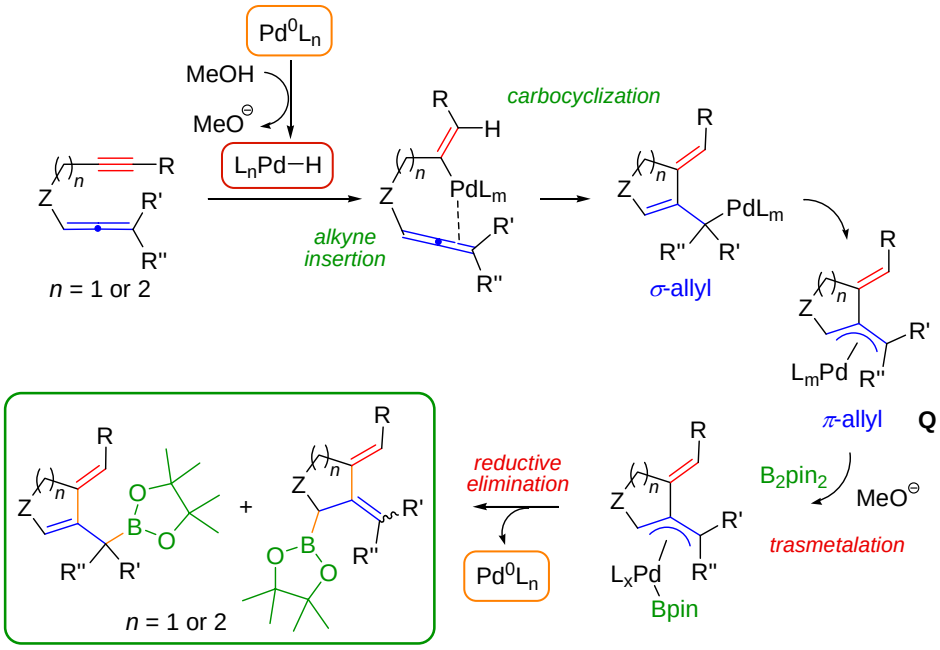
Figure 24. *X-ray diffraction structure from allylboronate* ***(E)-65c****.*

Furthermore, the methylene-bridged 1,6-allenyne **63e** performed the reaction leading to the allylboronate **64e** in low yield (12%, *Scheme 45*), thus demostrating one more time the importance of the Ingold-Thorpe effect in this kind of cyclization reactions.



Scheme 45. *Borylation cyclization of methylene-bridge 1,6-allenyne* ***63e***.

Regarding to the mechanistic pathway, the reaction probably starts with the formation of a Pd-hydride complex by protonation of Pd(0) intermediates with the alcohol, which promotes the hydropalladation of the alkyne. Subsequent carbometalation of the allene by the alkenylpalladium intermediate would take place regioselectively with formation of the new C–C bond onto the central carbon of the allene, and would give rise to allyl-Pd intermediate **Q** (*Scheme 46*).



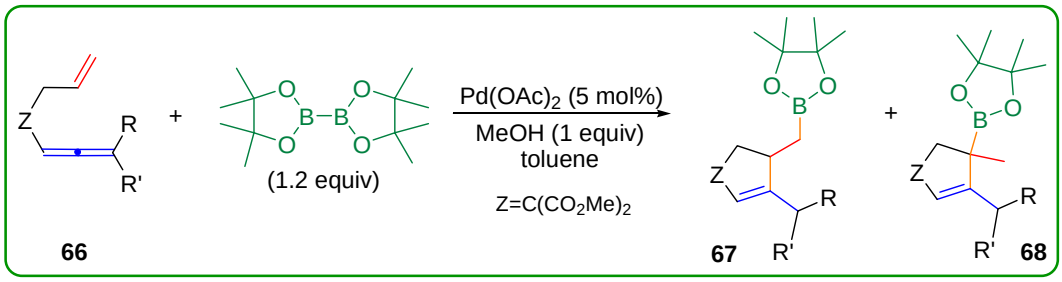
Scheme 46. *Proposed mechanistic pathway for allenynes.*

[246] (a) Beesley, R. M.; Ingold, C. K.; Thorpe, J. F. *J. Chem. Soc., Trans.* **1915**, *107*, 1080-1106. (b) Jung, M.; Piizzi, G. *Chem. Rev.* **2005**, *105*, 1735-1766.

Methoxide-promoted transmetalation of **Q** with bis(pinacolato)diboron, followed by reductive elimination would lead to the observed final products **61** and **62** (n = 1) or **64** and **65** (n = 2). Therefore, the regioslective outcome of the reaction is a consequence of the relative feasibility of both possible C–C reductive eliminations on the allylpalladium intermediate **Q**. In the cases in which exocyclic boronate was formed and additional stabilization coming from the coordination between the allyl-Pd intermediate and the new exocyclic double bond could be taking place.

Finally, it is wothwhile to note that high yields were obtained both 1,5- and 1,6-allenynes, despite the potential *β*-hydrogen elimination that could take place on the intermediates.

On the other hand, the extension of the borylative cyclization reaction to enallenes was also approached. Thus, when 1,5-enallene **66** was subjected under optimized conditions, the following mixture of alkyl- and allylboronates, **67** and **68**, were obtained (*Scheme 47*).[255]



***Scheme 47**. Pd-catalyzed cyclization/borylation of 1,5-enallenes.*

In some case this boronates mixture was obtained along with the cycloisomerization product **69** (*Figure 25*).

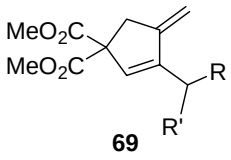
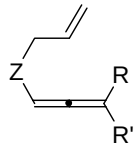
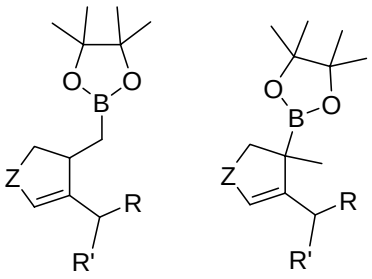


***Figure 25**. Cyloisomerization product **69**.*

[255] Pardo-Rodríguez, V.; Marco-Martínez, J.; Buñuel, E.; Cárdenas, D. J. *Org. Lett.* **2009**, *11*, 4548-4551.

Thereby, 1,5-enallenes **66a**,**b** performed the reaction leading to the boronates mixtures, **67a**,**b** and **68a**,**b**, in moderate yields (ca. 60%) although an additional 20% of cycloisomerization product **69a**,**b** was yielded for each case (*Table 14*).

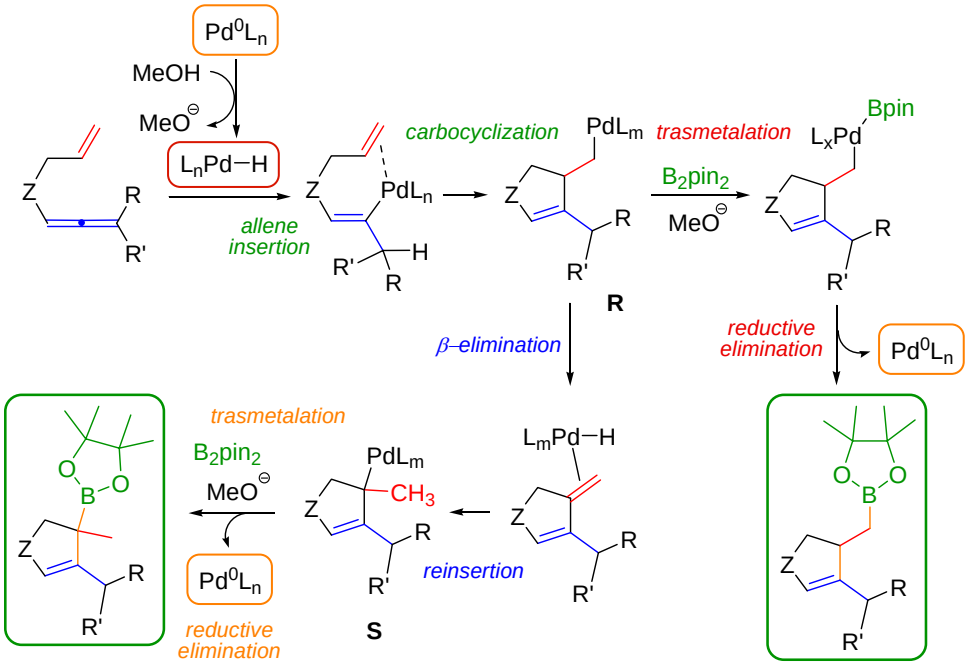
	substrate	T (ºC)	time (h)	yield (%)[a] / ratio
		Z = $C(CO_2Me)_2$		
1	**66a :** R = R' = Me	70	3	63[b] / **67a:68a**[c] (82:18)
2	**66b :** R = Me, R' = Et	50	16	61[b] / **67b:68b**[c] (49:51)

[a] *β*-Elimination products **69a** and **69b** were obtained in additional 20& yield each.
[b] Yields calculated by NMR.
[c] Approximate yield since these compounds contain pinal resulting from decomposition.

Table 14. *Alkyl- and allylboronates from 1,5-enallenes.*

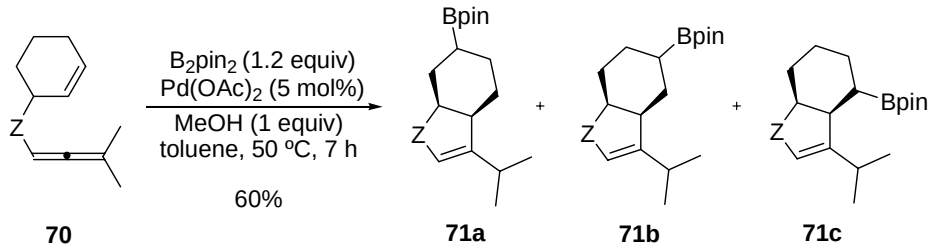
The reaction outcome indicated the occurrence of a different mechanism than described for the case of allenynes. In this case, the mechanistic pathway probably starts with the hydropalladation of the terminal double bond of the allene moeity resulting in a vinyl-Pd intermediate. Then, insertion of the alkene into the C–Pd bond would give **R** (*Scheme 48*). Finally, transmetalation of **R** with the boron reagent and reductive elimination would lead to alkylboronate **66**.

The formation of the regioisomer **68** could be explained by a *β*-hydrogen elimination in the alkylpalladium intermediate **R** and subsequent hydropalladation of the exocyclic alkene with the opposite regioselectivity to give **S** (*Scheme 48*). Transmetalation and reductive elimination would afford compound **68**. This proposal is consistent with the isolation of cycloisomerization compounds **69a-b**.



Scheme 48. *Proposed mechanistic pathway for enallenes.*

Moreover, the enallene **70** used by Bäckvall and coworkers,[241f] was also subjected to the reaction conditions giving rise to a mixture of three alkylboronates (**71**) located around the initial cyclohexene moiety, due to the possibility of consecutive *β*-hydrogen eliminations and reinsertions in this ring (*Scheme 49*). The three regioisomers **71a**, **71b**, and **71c** were separated by column chromatography (relative configuration of each isomer were determined by NOESY experiments).



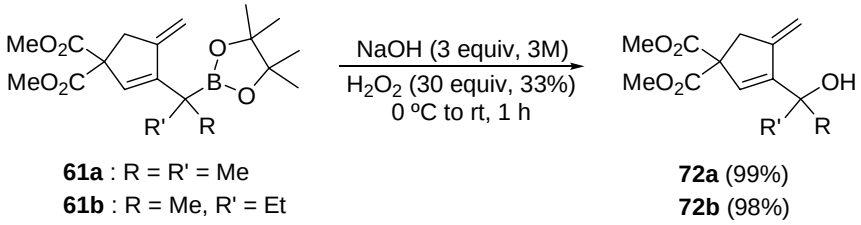
Scheme 49. *Borylative cyclization of cyclohexene-allene* ***70***.

[241] (f) Närhi, K.; Franzén, J.; Bäckvall J.-E. *Chem. Eur. J.* **2005**, *11*, 6937-6943.

All these results showed the different reactivity between alkyne, allene and alkene moieties regarding to hydropalladation process, being alkyne more reactive than allene, and the latter more reactive than alkene.

Finally, and with the aim of demonstrating the utility of these boronate compounds in further functionalizations, allylboronates **61a** and **61b** were subjected to oxidation, and to reaction with aldehydes in the presence of Lewis acids.[,124]

Thereby, allylalcohols **72a** and **72b** were obtained in almost quantitative yields (*Scheme 50*) when allylboronates **61a** and **61b** were transformed under alkaline aqueous conditions[b] in the presence of a large excess of oxygen peroxyde (33% w/v).



61a : R = R' = Me
61b : R = Me, R' = Et

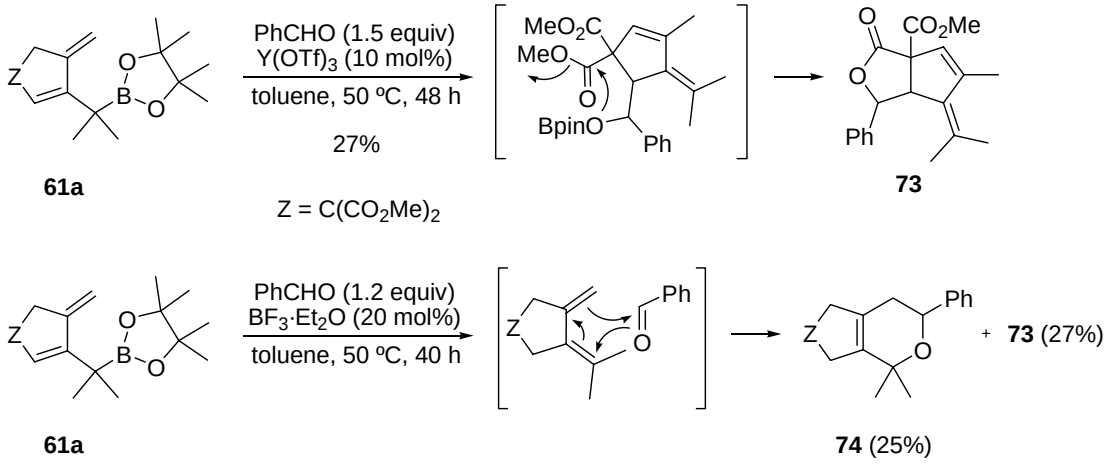
72a (99%)
72b (98%)

Scheme 50. *Synthesis of allylalcohols.*

Allylation reaction of benzaldehyde with **61a** in the presence of different Lewis acids ($Y(OTf)_3$ or $BF_3{\cdot}Et_2O$) provided lactone **73** in low yields (ca. 27%) as a result of the intramolecular transesterification between the alcohol resulting from the allylation and one of the ester groups (*Scheme 51*).

Moreover, the same compound **73** was obtained along with heterocyclic derivative **74** when $BF_3{\cdot}Et_2O$ was used. The latter could be the result of a Lewis acid catalyzed hetero Diels-Alder reaction of the aldehyde with a conjugated diene formed by decomposition of the boronate (*Scheme 51*).

[91] (b) Snyder, H. R.; Kuck, J. A.; Johnson, J. R. *J. Am. Chem. Soc.* **1938**, *60*, 105-111.
[122] (a) Hall, D. G. *Synlett* **2007**, 1644-1655. (b) Carosi, L.; Lachance, H.; Hall, D. G. *Tetrahedron* **2005**, *46*, 8981-8985.
[124] Rauniyar, V.; Hall, D. G. *J. Am. Chem. Soc.* **2004**, *126*, 4518-4519.

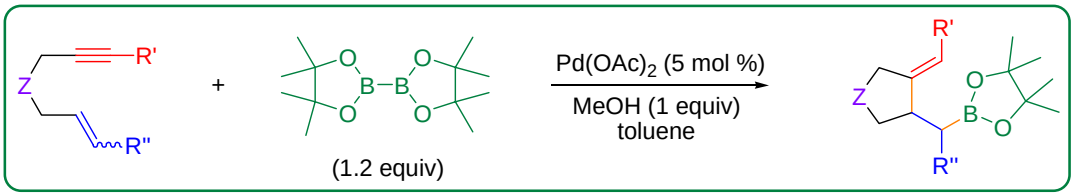


Scheme 51. *Lewis acid-catalyzed allylation reactions of* ***61a***.

In summary, a formal hydroborylative carbocyclization reaction of allenynes and enallenes in which formation of one C–C and one C–B bonds affords allylboronates and alkylboronates in smooth conditions has been developed. The reaction outcome implies that different mechanisms operate for the reactions of allenynes and enallenes, respectively, since the actual pathway depending on the relative reactivity of the alkyne or the alkene versus the allene moiety being, in general, a regioselective process. The cyclized boronates obtained can be functionalizated by oxidation or allylation reaction with aldehydes.

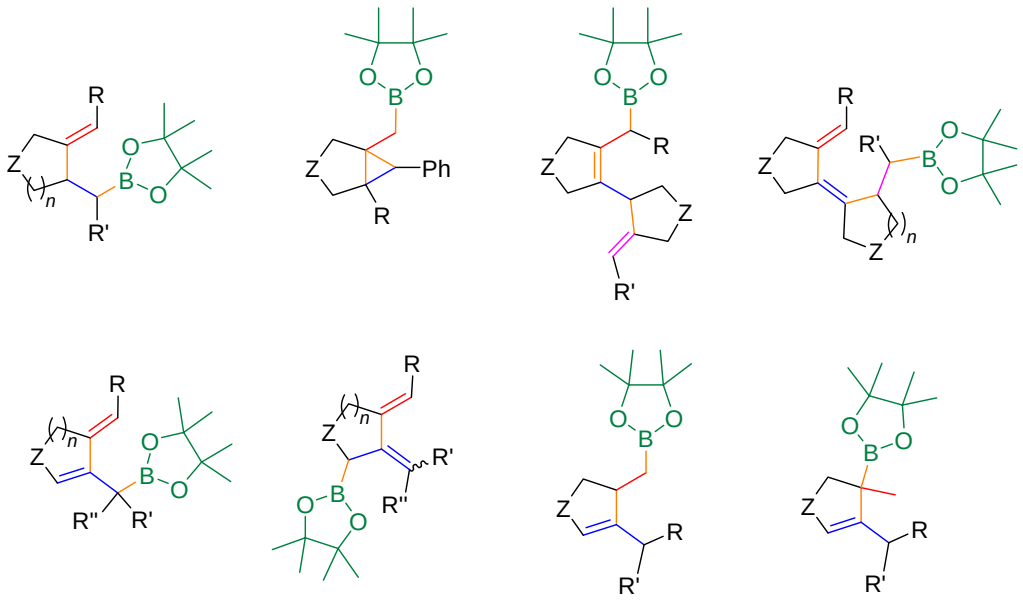
CONCLUSIONS

A new borylative cyclization process in which new C–C and C–B bonds are formed consecutively has been developed.



In the case of enynes, the trasmetallation process of B_2pin_2 seems to be faster than a possible *β*-hydrogen elimination.

A large number of different alkyl- and allylboronates have been prepared stereoselectively with moderate to good yields.

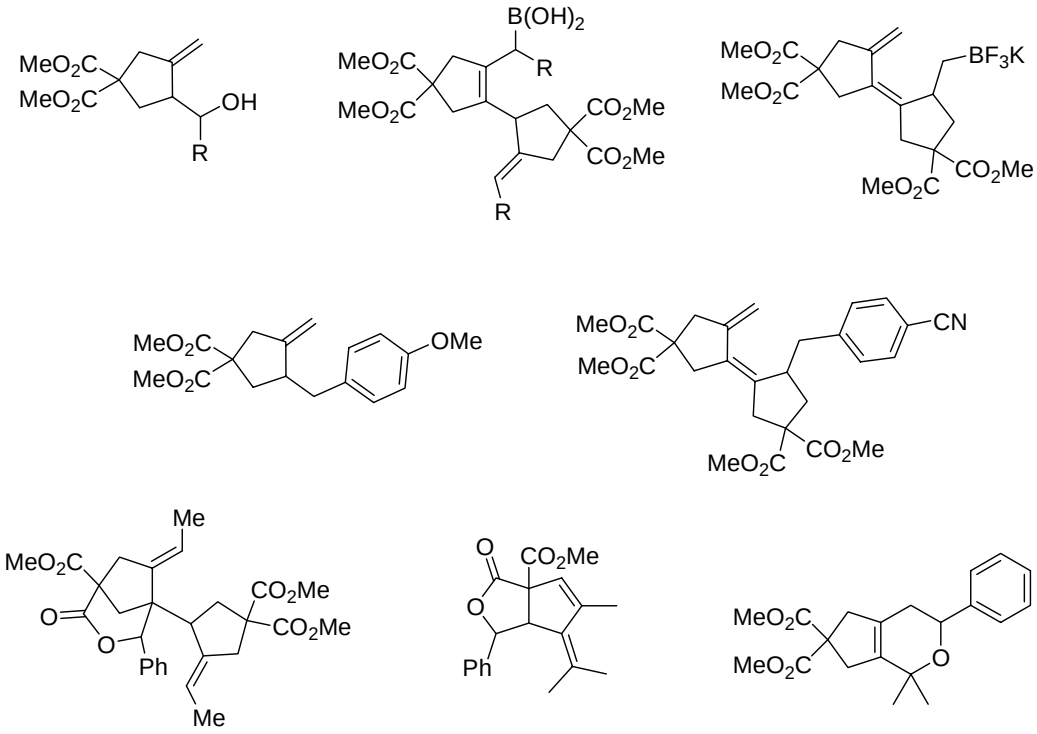


The reaction takes place in smooth conditions and is compatible with a wide variety of functional groups since avoids the use of highly nucleophilic or basic reagents for the synthesis of new boron compounds.

The formation of new asymmetric centers stereoespecifically and the configuration of new exocyclic double bonds in *E* configuration have been demonstrated. Moreover, in many cases, high leves of regioselectivity have been achieved.

The reaction allows the formation of one or two consecutive cycles in a cascade process with low charge of catalyst and in ligandless conditions.

In addition to the low toxicity of boron compounds, the new C–B bond formed in the reaction allows the application of these substrates to the synthesis of more complex molecules by further functionalization, such as oxidation to alcohols, trifluoroborate salts or boronic acids formation, allylation or Suzuki cross-coupling reactions. By this way, some new functionalized products have been obtained with good yields.



New applications of the prepared boronates, and deeper studies to clarify the mechanistic pathways are currently in progress.

EXPERIMENTAL SECTION

Contents ***Page***

1. General Materials and Methods

Solvents were purified by standard methods, and commercially available reagents were used without additional purification. Reagents were weighted on air, and reactions were performed under Ar. Subsequent work-up was performed on air.

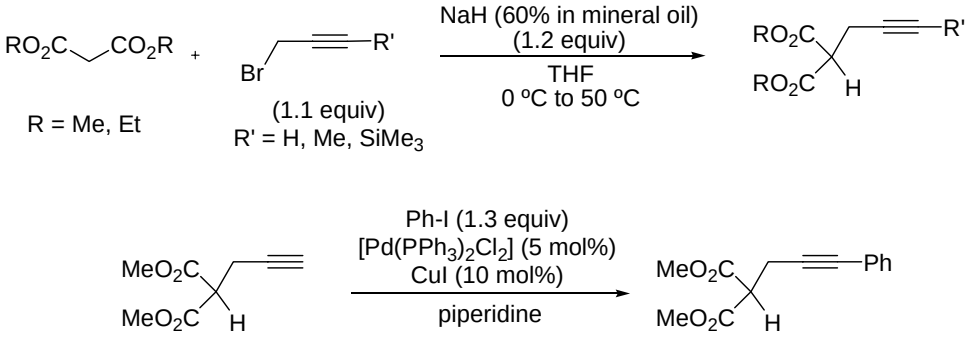
For preparation of starting materials, THF (SDS, anhydrous, analytical grade), and DMF (SDS, anhydrous, analytical grade), and for the borylative cyclization reactions, toluene (SDS, anhydrous, analytical grade) were dried by standing with activated 4Å molecular sieves for several days prior to use. Anhydrous MeOH (Scharlau, HPLC grade) was also stored with 4Å molecular sieves. Bis(pinacolato)diboron (Aldrich) was used as received and stored under Ar at 4ºC.

Thin layer chromatography was carried out using TLC-aluminium sheets with 0.2 mm of silica gel (Merck, TLC Silica gel 60 F_{254}). Chromatographic purifications were carried out using flash grade silica gel (Carlo Erba reagents-SDS S. A., Chromatogel 60 ACC, 40-60 μm).

NMR spectra were recorded at 23 $^{\circ}$C on the following spectrometer: Bruker AC-300 (300 MHz in ^{1}H, and 75 MHz in ^{13}C) in deuterated chloroform with the solvent signal serving as internal standard at 7.26 ppm in ^{1}H-NMR and 77.2 ppm in ^{13}C-NMR. The coupling constants (J) are reported in Hz and the chemical shifts (δ) in ppm. In the case of molecules containing boron, the α-carbon to the boron was determined by HMQC experiments since this carbon does not appear in ^{13}C-NMR due to the quadrupolar moment of the boron nucleous.

Mass spectra (FAB, EI and Electrospray) were reported on a GCT Walters spectrometer coupled to a chromatogram of gases (model 6890N of a Agilent technologies). Melting points were determined using a Gallenkamp apparatus.

Dimethyl propargylmalonate (Fluka) was used as received and stored at 4 ºC. Dimethyl allylmalonate (Aldrich) and diethyl malonate (Aldrich), were used as received and stored at r.t. Dialkyl propargylmalonate derivatives were prepared by alkylation of corresponding malonate derivatives or by Sonogashira coupling, following the next general procedures:



Characterization and experimental data of these compounds have been already reported in the literature following the same, analogous, or other preparation methods and will be noted in each case. Dimethyl malonate (Aldrich), and dimethyl propargyl malonate (Fluka) were purchased.

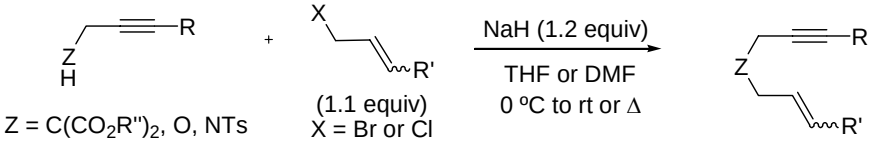
The usual extractive work-up refers to proportioning of the crude reaction between an organic solvent and water, phase separation, drying (over anhydrous Na_2SO_4 and/or $MgSO_4$), and evaporation under reduced pressure.

2. Pd-Catalyzed Borylative Cyclization of 1,6-Enynes to Alkylboronates

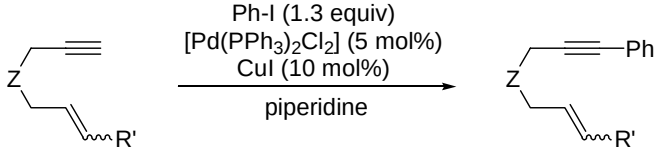
Most of allyl derivatives used as electrophiles have been already described and characterized in the literature, and were prepared following related procedures that will be cited in each case. Some of them were purchased: 3-bromoprop-1-ene or allyl bromide (Aldrich), 3-chloro-2-methylprop-1-ene (Aldrich), 4-bromobut-1-ene (Aldrich), 5-bromopent-1-ene (Aldrich), and (*E*)-(3-bromoprop-1-enyl)benzene or cinnamyl bromide (Aldrich).

2.1 Preparation and experimental data of enynes

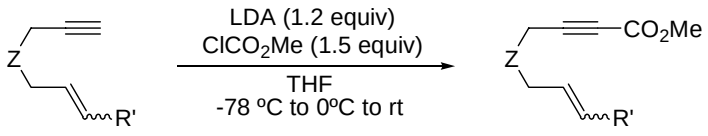
Mainly, three different procedures were used to the synthesis of enynes:



Procedure A: *General procedure for alkylation of malonate derivatives, bis(sulfonyl)methane derivatives, alcohols and 4-toluenesulfonamides:* To a suspension of NaH (60% in mineral oil, 1.2 equiv) in anhydrous THF or DMF (solvent and volume will be indicated in each case) under Ar atmosphere at 0 ºC, was slowly added the corresponding nucleophile (1 equiv) and the mixture was stirred at rt for 5-10 min. (formation of H_2 bubbles were observed during the addition). Then, the corresponding electrophile (1.0-1.2 equiv) was added dropwise and the mixture was allow to reaction at rt or heated (will be specified in each case). Screening by TLC indicated the completion of the reaction. Then, in the case of THF, most of the solvent was removed under vacuum and later, water and Et_2O were added into the resulting mixture. The aqueous layer was separated and extracted successively with Et_2O. In the case of DMF, similar extractive work-up with Et_2O/aq. solution of HCl (5-10%). The combined organic phases were dried over anhydrous Mg_2SO_4 and filtered through anhydrous Na_2SO_4. The solvent was removed under vacuum and the residue was purified by column chromatography (hexane/EtOAc).

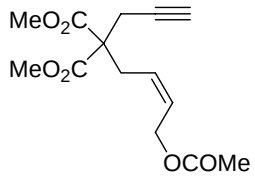


Procedure B: *General procedure for Sonogashira cross-couplings:* CuI (10 mol%), and $[Pd(PPh_3)_2Cl_2]$ (5 mol%) were suspended in piperidine, and stirred for 5 min. Then, iodobenzene (1.3 equiv) and a solution of the enyne (1 equiv) in piperidine were added sequentially. The reaction was stirred at rt (unless other temperature was specify in each case) until TLC show total conversion. Then, the crude was dissolved in Et_2O and extracted with Et_2O/aq. solution of HCl (5-10%). The combined organic phases were dried over anhydrous Mg_2SO_4 and filtered through anhydrous Na_2SO_4. The solvent was removed under vacuum and the residue was purified by column chromatography (hexane:EtOAc).



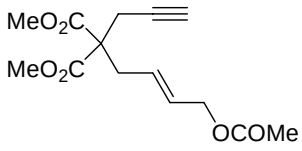
Procedure C: *General procedure for methoxy acylation of enynes:* To a solution of di-*iso*-propylamine (1.8 equiv) in anhydrous THF at -78 ºC, was added *n*-BuLi (2.5 M in hexanes, 1.2 equiv). The solution was warmed to 0 ºC for 15 min. and then recooled to -78 ºC. To the reaction mixture was slowly added a solution of enyne (1 equiv) in anhydrous THF. After stirring at -78 ºC for 1 h, the reaction mixture was treated with methyl chloroformate (1.5 equiv), stirred at -78 ºC for additional 30 min. and then warmed to rt. The reaction mixture was diluted with Et_2O, washed with sodium bisulphite (40% w/v), dried over over anhydrous Mg_2SO_4 and filtered through anhydrous Na_2SO_4. The solvent was removed under vacuum and the residue was purified by column chromatography (hexane:EtOAc).

(*Z*)-Dimethyl 2-(4-acetoxybut-2-enyl)-2-(prop-2-ynyl)malonate (1a)



Starting from dimethyl propargylmalonate (14.27 mmol, Fluka) and (*Z*)-4-bromobut-2-enyl acetate[256] (15,54 mmol) and following Procedure A for alkylations (DMF, 10 mL, 0ºC to 70ºC, 24 h), **1a** was obtained in 40% yield as a colorless oil. Characterization and experimental data of the compound were already reported following other procedure.[257]

(*E*)-Dimethyl 2-(4-acetoxybut-2-enyl)-2-(prop-2-ynyl)malonate ((*E*)-1a)

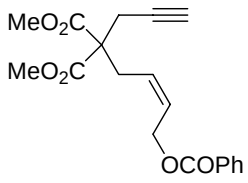


Starting from dimethyl propargylmalonate (7.06 mmol, Fluka) and (*E*)-4-bromobut-2-enyl acetate[258] (7.77 mmol) and following Procedure A for alkylations (DMF, 20 mL, 0ºC to 70ºC, 22 h), **(*E*)-1a** was obtained in 57% yield as a yellowish oil.

[256] Reppe, W. J. *Liebigs Ann. Chem.* **1935**, 80-158.
[257] Ihle, N. C.; Heathcock, C. H. *J. Org. Chem.* **1993**, *58*, 560-563.
[258] Zhao, L.; Lu, X.; Xu, W. *J. Org. Chem.* **2005**, *70*, 4059-4063.

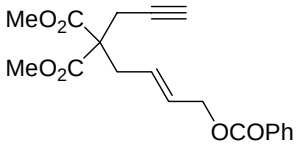
Characterization and experimental data of the compound were already reported following other procedure.

(*Z*)-Dimethyl 2-(4-(benzoyloxy)but-2-enyl)-2-(prop-2-ynyl)malonate (1b)



Starting from dimethyl propargylmalonate (15.7 mmol, Fluka) and (*Z*)-4-bromobut-2-enyl benzoate[259] (15.7 mmol) and following Procedure A for alkylations (DMF, 50 mL, 0ºC to 70ºC, 22 h), **1b** was obtained in 65% yield as a white solid. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.00 (m, 2H), 7.51 (m, 1H), 7.39 (m, 2H), 5.83 (m, 1H), 5.48 (m, 1H), 4.88 (d, J = 6.8 Hz, 2H), 3.71 (s, 6H), 2.94 (d, J =7.9 Hz, 2H), 2.80 (d, J =2.7 Hz, 2H), 2.03 (t, J = 2.7 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 170.2 (C), 166.6 (C), 133.2 (CH), 130.4 (C), 129.8 (CH), 128.8 (CH), 128.6 (CH), 127.6 (CH), 78.8 (CH), 72.1 (CH), 60.9 (CH_2), 57.0 (C), 53.2 (CH_3), 30.6 (CH_2), 23.0 (CH_2). HRMS-ESI+ $[MH]^+$ Calc. for $C_{19}H_{21}O_6$: 345.1332; found: 345.1343.

(*E*)-Dimethyl 2-(4-(benzoyloxy)but-2-enyl)-2-(prop-2-ynyl)malonate ((*E*)-1b)

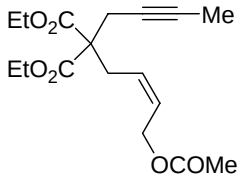


Starting from dimethyl propargylmalonate (7.13 mmol, Fluka) and (*E*)-4-bromobut-2-enyl benzoate (7.84 mmol) and following Procedure A for alkylations (DMF, 20 mL, 0ºC to 70ºC, 22h), **(*E*)-1b** was obtained in 62% yield as a yellowish oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.02 (m, 2H), 7.54 (m, 1H), 7.42 (m, 2H), 5.85 (m, 1H), 5.69 (m, 1H), 4.75 (d, J = 6.1 Hz, 2H), 3.72 (s, 6H), 2.84 (d, J =7.7 Hz, 2H), 2.80 (d, J =2.7 Hz, 2H), 2.03 (t, J = 2.6 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 170.1 (C), 166.3 (C),

[257] Ihle, N. C.; Heathcock, C. H. *J. Org. Chem.* **1993**, *58*, 560-563.
[259] Ashton, W. T.; Meurer, L. C.; Cantone, C. L.; Field, A. K. Hannah, J.; Karkas, J. D.; Liou, R.; Patel, G. F.; Perry, H. C. *J. Med. Chem.* **1988**, *31*, 2304-2315.

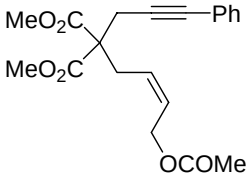
133.1 (CH), 130.3 (C), 129.7 (CH), 129.5 (CH), 128.8 (CH), 128.5 (CH), 78.7 (C), 71.8 (CH), 65.0 (CH_2), 57.0 (C), 52.9 (CH_3), 35.3 (CH_2), 23.0 (CH_2). HRMS-ESI+ $[MH]^+$ Calc. for $C_{19}H_{21}O_6$: 345.1332; found: 345.1341.

(*Z*)-Diethyl 2-(4-acetoxybut-2-enyl)-2-(but-2-ynyl)malonate (1c)



Starting from diethyl 2-(but-2-ynyl)malonate[260] (3.753 mmol) and (*Z*)-4-bromobut-2-enyl acetate (4.128 mmol) and following Procedure A for alkylations (THF, 5 mL, 0ºC to 60ºC, 24 h), 1c was obtained in 51% yield as a colorless oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 6.64 (m, 1H), 5.39 (m, 1H), 4.61 (dd, J = 7.0, 1.2 Hz, 2H), 4.14 (m, 4H), 2.79 (d, J = 7.9 Hz, 2H), 2.65 (c, J = 2.5 Hz, 2H), 1.99 (s, 3H), 1.69 (t, J = 2.5 Hz, 3H), 1.19 (t, J = 7.1 Hz, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 171.0 (C), 170.1 (C), 128.3 (CH), 128.0 (CH), 79.3 (C), 73.5 (C), 61.9 (CH_2), 60.6 (CH_2), 57.0 (C), 30.4 (CH_2), 23.2 (CH_2), 21.1 (CH_3), 14.3 (CH_3), 3.6 (CH_3). HRMS-FAB+ $[MH]^+$ Calc. for $C_{17}H_{25}O_6$: 325.1651; found: 325.1653.

(*Z*)-Dimethyl 2-(4-acetoxybut-2-enyl)-2-(3-phenylprop-2-ynyl)malonate (1d)

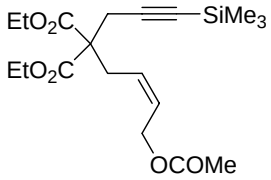


Starting from diethyl 2-(3-phenylprop-2-ynyl)malonate[261] (5.874 mmol) and (*Z*)-4-bromobut-2-enyl acetate (7.019 mmol) and following Procedure A for alkylations (THF, 10 mL, 0ºC to 50ºC, 20 h), **1d** was obtained in 63% yield as a colorless oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.39 (m, 2H), 7.29 (m, 3H), 5.76 (m, 1H), 5.54 (m, 1H),

[256] Reppe, W. J. *Liebigs Ann. Chem.* **1935**, 80-158.
[260] Brummond, K. M.; Chen, H.; Sill, P. C.; You, L. *J. Am. Chem. Soc.* **2002**, *124*, 15186-15187.
[261] Schiller, R.; Pour, M.; Fakova, H.; Kunes, J.; Cisarova, I. *J. Org. Chem.* **2004**, *69*, 6761-6765.

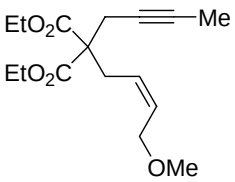
4.71 (dd, J = 7.0, 1.3 Hz, 2H), 3.78 (s, 6H), 3.05 (s, 2H), 2.98 (d, J = 7.9 Hz, 2H), 2.04 (s, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 170.9 (C), 170.3 (C), 131.9 (CH), 128.7 (CH), 128.5 (CH), 128.4 (CH), 127.7 (C), 123.2 (C), 84.2 (C), 84.1 (C), 60.3 (CH_2), 57.3 (C), 53.1 (CH), 30.7 (CH_2), 24.0 (CH_2), 21.1 (CH_2). HRMS-FAB+ $[MH]^+$ Calc. for $C_{20}H_{23}O_6$: 359.1494; found: 359.1497.

(*Z*)-Diethyl 2-(4-acetoxybut-2-enyl)-2-(3-(trimethylsilyl)prop-2-ynyl)malonate (1e)



Starting from diethyl 2-(3-(trimethylsilyl)prop-2-ynyl)malonate[262] (3.699 mmol) and (*Z*)-4-bromobut-2-enyl acetate (4.069 mmol) and following Procedure A for alkylations (THF, 6 mL, 0ºC to 65ºC, 15 h), **1e** was obtained in 48% yield as a colorless oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.67 (m, 1H), 5.41 (m, 1H), 4.63 (dd, J = 7.0, 1.0 Hz, 2H), 4.16 (m, 4H), 2.82 (d, J = 8.0 Hz, 2H), 2.75 (s, 2H), 2.01 (s, 3H), 1.22 (t, J = 7.2 Hz, 6H), 0.09 (s, 9H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 171.0 (C), 169.8 (C), 128.6 (CH), 127.9 (CH), 101.4 (C), 88.6 (C), 62.0 (CH_2), 60.5 (CH_2), 57.0 (C), 30.4 (CH_2), 24.3 (CH_2), 21.2 (CH_3), 14.3 (CH_3), 0.16 (CH_3). HRMS-FAB+ $[MH]^+$ Calc. for $C_{19}H_{31}O_6Si$: 383.1889; found: 383.1873.

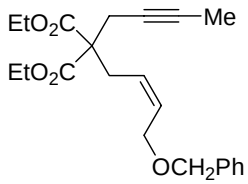
(*Z*)-Diethyl 2-(but-2-ynyl)-2-(4-methoxybut-2-enyl)malonate (1f)



[256] Reppe, W. J. *Liebigs Ann. Chem.* **1935**, 80-158.
[262] Brummond, K. M.; Chen, H.; Fisher, K. D.; Kereker, A. D.; Rickards, B.; Sill, P. C.; Geib, S. J. *Org. Lett.* **2002**, *4*, 1931-1934.

Starting from diethyl 2-(but-2-ynyl)malonate (2.237 mmol) and (*Z*)-1-bromo-4-methoxybut-2-ene[263] (2.684 mmol) and following Procedure A for alkylations (THF, 5 mL, 0ºC to 55ºC, 20 h), **1f** was obtained in 65% yield as a colorless oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.66 (m, 1H), 5.34 (m, 1H), 4.16 (m, 4H), 4.00 (d, J = 6.6 Hz, 2H), 3.29 (s, 3H), 2.79 (d, J = 7.9 Hz, 2H), 2.68 (c, J = 2.5 Hz, 2H), 1.72 (t, J = 2.5 Hz, 3H), 1.21 (t, J = 7.0, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 170.3 (C), 131.2 (CH), 126.2 (CH), 79.1 (C), 73.8 (C), 68.4 (CH_2), 61.9 (CH_2), 58.2 (CH_3), 57.2 (C), 30.5 (CH_2), 23.2 (CH_2), 14.3 (CH_3), 3.7 (CH_3). HRMS-FAB+ $[MH]^+$ Calc. for $C_{16}H_{25}O_5$: 297.1701; found: 297.1693.

(*Z*)-Diethyl 2-(4-(benzyloxy)but-2-enyl)-2-(but-2-ynyl)malonate (1g)



Starting from diethyl 2-(but-2-ynyl)malonate (4.691 mmol) and (*Z*)-((4-bromobut-2-enyloxy)methyl)benzene[264] (5.629 mmol) and following Procedure A for alkylations (THF, 10 mL, 0ºC to 60ºC, 24 h), **1g** was obtained in 72% yield as a yellowish oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.27-7.15 (m, 5H), 5.69 (m, 1H), 5.31 (m, 1H), 4.42 (s, 2H), 4.09 (m, 6H), 2.74 (d, J = 7.7 Hz, 2H), 2.64 (c, J =2.6 Hz, 2H), 1.62 (t, J = 2.6 Hz, 3H), 1.14 (t, J = 7.1, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 170.2 (C), 138.6 (C), 131.3 (CH), 128.6 (CH), 128.0 (CH), 127.8 (CH), 126.1 (CH), 79.0 (C), 73.8 (C), 72.6 (CH_2), 66.2 (CH_2), 61.7 (CH_2), 57.1 (C), 30.5 (CH_2), 23.1 (CH_2), 14.3 (CH_3), 3.6 (CH_3). HRMS-FAB+ $[MH]^+$ Calc. for $C_{22}H_{29}O_5$: 373.2014; found: 373.2000.

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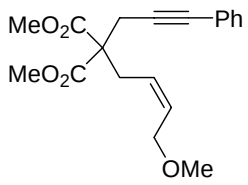
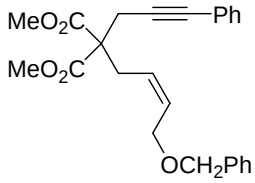
[260] Brummond, K. M.; Chen, H.; Sill, P. C.; You, L. *J. Am. Chem. Soc.* **2002**, *124*, 15186-15187.
[263] Heasley, V. L.; Gipe, R. K.; Martin, J. D.; Wiere, H. C.; Oaker, M. L.; Shellhamer, D. F.; Heasley, G. E.; Robinson, B. L. *J. Org. Chem.* **1983**, *48*, 3195-3199.
[264] Gorst-Allman, C. P.; Steyn, P. S. *J. Chem. Soc., Perkin Trans. 1*, **1987**, 163-168.

(*Z*)-Dimethyl 2-(4-methoxybut-2-enyl)-2-(3-phenylprop-2-ynyl)malonate (1h)



Starting from dimethyl 2-(3-phenylprop-2-ynyl)malonate[261] (2.84 mmol) and (*Z*)-1-bromo-4-methoxybut-2-ene (3.41 mmol) and following Procedure A for alkylations (THF, 16 mL, 0 ºC to rt, 48 h), **1h** was obtained in 54% yield as a yellowish oil. Characterization and experimental data of the compound were already reported following analogous procedure.[265]

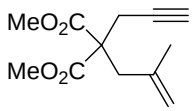
(*Z*)-Dimethyl 2-(4-(benzyloxy)but-2-enyl)-2-(3-phenylprop-2-ynyl)malonate (1i)



Starting from dimethyl 2-(3-phenylprop-2-ynyl)malonate[261] (2.84 mmol) and (*Z*)-((4-bromobut-2-enyloxy)methyl)benzene (3.41 mmol) and following Procedure A for alkylations (THF, 16 mL, 0 ºC to rt, 48 h), **1i** was obtained in 39% yield as a yellowish oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.25-7.12 (m, 10H), 5.70 (m, 1H), 5.32 (m, 1H), 4.33 (s, 2H), 4.04 (d, J = 6.1 Hz, 2H), 3.61 (s, 6H), 2.83 (d, J = 7.8 Hz, 2H), 2.92 (s, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 170.3 (C), 138.3 (C), 131.8 (CH), 131.7 (CH), 128.5 (CH), 128.4 (CH), 128.3 (CH), 127.9 (CH), 127.8 (CH), 125.7 (CH), 123.2 (C), 84.5 (C), 83.8 (C), 72.5 (CH_2), 66.0 (CH_2), 57.2 (C), 53.0 (CH_3), 30.7 (CH_2), 23.8 (CH_2). HRMS-FAB+ $[MH]^+$ Calc. for $C_{25}H_{27}O_5$: 407.1858; found: 407.1848.

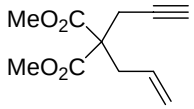
[261] Schiller, R.; Pour, M.; Fakova, H.; Kunes, J.; Cisarova, I. *J. Org. Chem.* **2004**, *69*, 6761-6765.
[263] Heasley, V. L.; Gipe, R. K.; Martin, J. D.; Wiere, H. C.; Oaker, M. L.; Shellhamer, D. F.; Heasley, G. E.; Robinson, B. L. *J. Org. Chem.* **1983**, *48*, 3195-3199.
[264] Gorst-Allman, C. P.; Steyn, P. S. *J. Chem. Soc., Perkin Trans. 1*, **1987**, 163-168.
[265] Miura, T.; Shimada, M.; Murakami, M. *J. Org. Chem.* **2005**, *127*, 1094-1095.

Dimethyl 2-(2-methylallyl)-2-(prop-2-ynyl)malonate (1j)



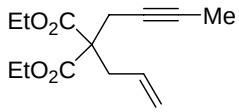
Starting from dimethyl propargylmalonate (11.75 mmol, Fluka) and 3-chloro-2-methylprop-1-ene (11.75 mmol, Aldrich) and following Procedure A for alkylations (DMF, 5 mL, 0ºC to rt, 6 h), **1j** was obtained in 59% yield as a white solid. Characterization and experimental data of the compound were already reported following other procedure.[266]

Dimethyl 2-allyl-2-(prop-2-ynyl)malonate (1k)



Starting from dimethyl propargylmalonate (Fluka) and 3-bromoprop-1-ene (Aldrich) and following Procedure A for alkylations (THF, 60 mL, 0 ºC to 50 ºC, 17 h), **1k** was obtained in 86% yield as a colorless oil. Characterization and experimental data of the compound were already reported following analogous procedure.[267]

Diethyl 2-allyl-2-(but-2-ynyl)malonate (1l)

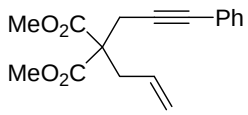


Starting from diethyl 2-(but-2-ynyl)malonate (4.691 mmol) and 3-bromoprop-1-ene (5.629 mmol, Aldrich) and following Procedure A for alkylations (THF, 10 mL, 0ºC to 50ºC, 20 h), **1l** was obtained in 75% yield as a colorless oil. Characterization and

[260] Brummond, K. M.; Chen, H.; Sill, P. C.; You, L. *J. Am. Chem. Soc.* **2002**, *124*, 15186-15187.
[266] Gomez, A. M.; Company, M. D.; Valverde, S.; Lopez, J. C. *Org. Lett.* **2002**, *4*, 383-386.
[267] Miura, K. Saito, H.; Fujisawa, N.; Hosomi, A. *J. Org. Chem.* **2000**, *65*, 8119-8122.

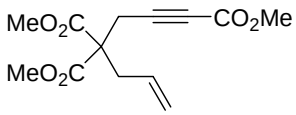
experimental data of the compound were already reported following analogous procedure.[268]

Dimethyl 2-allyl-2-(3-phenylprop-2-ynyl)malonate (1m)



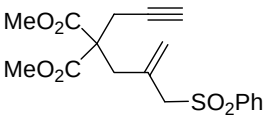
Starting from enyne **1k** (2.85 mmol) and iodobenzene (3.71 mmol, Aldrich) and following Procedure B for Sonogashira cross-coupling (piperidine, 6 mL, 38 h), **1m** was obtained in 76% yield as a yellowish oil. Characterization and experimental data of the compound were already reported following other procedure.[269]

Trimethyl hept-6-en-1-yne-1,4,4-tricarboxylate (1n)



Starting from enyne **1k** (1.90 mmol) and methyl chloroformate (1.78 mmol, Aldrich) and following Procedure C (THF, 8 mL, 24 h), **1n** was obtained in 82% yield as a pale yellowish oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.59 (m, 1H), 5.22-5.10 (m, 2H), 3.74 (s, 3H), 3.73 (s, 3H), 3.72 (d, J = 1.1 Hz, 2H), 2.92 (m, 2H), 2.78 (dd, J = 7.5, 0.9 Hz, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 169.7 (C), 153.8 (C), 131.3 (CH), 120.6 (CH_2), 83.7 (C), 75.5 (C), 56.7 (C), 53.1 (CH_3), 52.8 (CH_3), 37.0 (CH_2), 23.1 (CH_2). HRMS-ESI+ $[MH]^+$ Calc. for $C_{13}H_{17}O_6$: 269.1019; found: 269.1027.

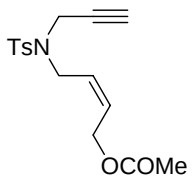
Dimethyl 2-(2-(phenylsulfonylmethyl)allyl)-2-(prop-2-ynyl)malonate (1o)



[268] Maremoto, T.; Fuji, K.; Tsutsumi, K.; Kakiuchi, K. *J. Am. Chem. Soc.* **2002**, *124*, 3806-3807.
[269] Park, K. H.; Cheng, Y. K. *Adv. Synth. Catal.* **2005**, *347*, 854-866.

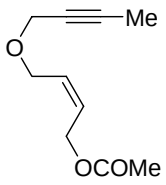
Starting from dimethyl propargylmalonate (1.32 mmol, Fluka) and (2-(chloromethyl)allylsulfonyl)benzene[270] (1.45 mmol) and following Procedure A for alkylations (DMF, 5 mL, 0ºC to rt, 20 h), **1o** was obtained in 72% yield as a white solid (mp 106-109 ºC). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.86(m, 2H), 7.65 (m, 1H), 7.54 (m, 2H), 5.17 (s, 1H), 5.00 (s, 1H), 3.76 (s, 2H), 3.73 (s, 6H), 2.91 (s, 2H), 2.74 (d, J = 2.7 Hz), 2.06 (t, J = 2.7 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 170.4, 138.6, 134.2, 132.4, 129.4, 129.0, 125.9, 78.9, 72.9, 63.1, 57.4, 53.3, 37.3, 23.4. HRMS-ESI+ $[MH]^+$ Calc. for $C_{18}H_{21}O_6S$: 365.1053; found: 365.1058.

(*Z*)-4-(4-Methyl-*N*-(prop-2-ynyl)phenylsulfonamido)but-2-enyl acetate (1r)



Starting from *N*-2-propynyl-(4-toluene)sulfonamide[271] (2.39 mmol) and (*Z*)-4-bromobut-2-enyl acetate (2.63 mmol) and following Procedure A for alkylations (THF, 30 mL, 0ºC to 50 ºC, 26 h), **1r** was obtained in 79% yield as a yellowish oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.11 (m, 4H), 7.73 (m, 2H), 7.59 (m, 4H), 5.88 (m, 2H), 4.63 (d, J = 6.5 Hz, 2H), 3.19 (d, J = 2.7 Hz, 2H), 3.16 (d, J = 6.7 Hz, 2H), 2.09 (m, 1H), 2.07 (s, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 171.1 (C), 136.6 (C), 135.3 (CH), 131.9 (CH), 129.1 (CH), 128.7 (CH), 125.3 (CH), 88.8 (C), 75.9 (CH), 74.8 (CH), 60.7 (CH_2), 27.9 (CH_2), 21.3 (CH_3), 21.1 (CH_2). HRMS-FAB+ $[M]^+$ Calc. for $C_{16}H_{19}NO_4S$: 322.1113; found: 322.1121.

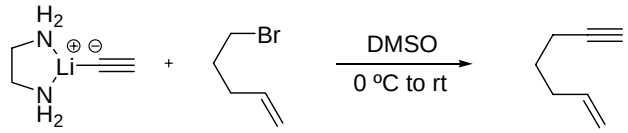
(*Z*)-4-(But-2-ynyloxy)but-2-enyl acetate (1s)



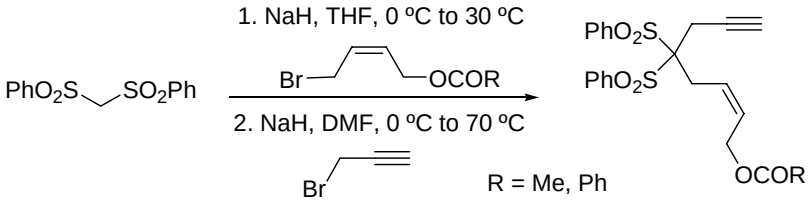
[256] Reppe, W. J. *Liebigs Ann. Chem.* **1935**, 80-158.
[270] Li, X.; Lantrip, D.; Fuchs, P. L. *J. Am. Chem. Soc.* **2003**, *125*, 14262-14263.
[271] Oppolzer, W.; Bedoya-Zurita, M.; Switzer, C. Y. *Tetrahedron Lett.* **1988**, *29*, 6433-6436.

Starting from diethyl but-2-yn-1-ol (5.849 mmol, Aldrich) and (*Z*)-4-bromobut-2-enyl acetate and following Procedure A for alkylations (THF, 30 mL, 0ºC to 50 ºC, 20 h), **1s** was obtained in 45% yield as a colorless oil. Characterization and experimental data of the compound were already reported following analogous procedure.[272]

Hept-1-en-6-yne (1t)



Starting from lithium acetylide ethylenediamine complex (50.63 mmol, Aldrich) and 5-bromopent-1-ene (33.75 mmol, Aldrich) and according to literature procedure[273] in DMSO (20 mL, 0 ºC (1 h) to rt (2 h)), **1t** was obtained in 34% yield as a colorless oil. Characterization and experimental data of the compound were already reported.



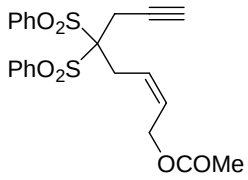
(*Z*)-5,5-Bis(phenylsulfonyl)pent-2-enyl acetate

To a suspension of NaH (60% in mineral oil, 8.1 mmol, 1.2 equiv), in THF (25 mL) at 0 ºC was added a solution of 1,1-bis(phenylsulfonyl)methane (6.75 mmol, 1equiv, Aldrich) and (*Z*)-4-bromobut-2-enyl acetate (7.42 mmol, 1.1 equiv) and the mixture was stirred at rt for 16 h. After extractive work-up (Et_2O/saturated solution of NH_4Cl), the residue was chromatographed (EtOAc: hexane) leading to sticky light orange solid in 76%. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.95-7.91 (m, 4H), 7.72-7.65 (m, 2H), 7.59-7.51 (m, 4H), 5.72-5.42 (m, 2H), 4.66 (t, J = 6.3 Hz, 1H), 4.47 (d, J = 7.0 Hz, 2H), 2.99 (t, J

[256] Reppe, W. J. *Liebigs Ann. Chem.* **1935**, 80-158.
[272] Zhang, Q.; Xu, W.; Lu, X. *J. Org. Chem.* **2005**, *70*, 1505-1507.
[273] (a) Negishi, E.; Holmes, S. J.; Tour, J. M.; Miller, J. A.; Cederbaum, F. E.; Swanson, D. R.; Takahashi, T. *J. Am. Chem. Soc.* **1989**, *111*, 3336-3346. (b)Himes, R. A.; Fanwick, P. E.; Rothwell, I. P. *Chem. Comm.* **2003**, 18-19.

= 6.3 Hz, 2H), 2.03 (s, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 170.7, 137.7, 134.7, 129.6, 129.1, 127.9, 127.4, 83.2, 59.7, 23.8, 20.9.

(*Z*)-5,5-Bis(phenylsulfonyl)oct-2-en-7-ynyl acetate (1u)



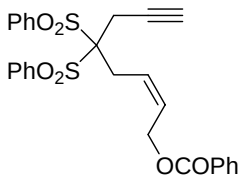
Starting from (*Z*)-5,5-Bis(phenylsulfonyl)pent-2-enyl acetate (4.41 mmol) and propargyl bromide (80 % in tolene, 5.29 mmol) and following Procedure A for alkylations (DMF, 50 mL, 0ºC to 70 ºC, 21 h), **1u** was obtained in 49% yield as a yellowish oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.11 (m, 4H), 7.73 (m, 2H), 7.59 (m, 4H), 5.88 (m, 2H), 4.63 (d, *J* = 6.5 Hz, 2H), 3.19 (d, *J* = 2.7 Hz, 2H), 3.16 (d, *J* = 6.7 Hz, 2H), 2.09 (m, 1H), 2.07 (s, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 171.1 (C), 136.6 (C), 135.3 (CH), 131.9 (CH), 129.1 (CH), 128.7 (CH), 125.3 (CH), 88.8 (C), 75.9 (CH), 74.8 (CH), 60.7 (CH_2), 27.9 (CH_2), 21.3 (CH_3), 21.1 (CH_2). HRMS-FAB+ $[M]^+$ Calc. for $C_{22}H_{22}O_6S_2$: 447.0936; found: 447.0937.

(*Z*)-5,5-Bis(phenylsulfonyl)pent-2-enyl benzoate

Following the same procedure and quantities as mentioned before for (*Z*)-5,5-bis(phenylsulfonyl)pent-2-enyl acetate using (*Z*)-4-bromobut-2-enyl benzoate, the corresponding desired product was obtained as a white solid in 76% yield. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.01 (d, *J* = 7.1 Hz, 2H), 7.95 (d, *J* = 7.7 Hz, 4H), 7.64 (t, *J* = 7.4 Hz, 2H), 7.52 (m, 5H), 7.43 (t, *J* = 7.7 Hz, 2H), 5.74 (m, 2H), 4.82 (t, *J* = 6.1 Hz, 1H), 4.71 (d, *J* = 6.0 Hz, 2H), 3.09 (t, *J* = 6.3 Hz, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 166.5 (C), 138.1 (C), 134.9 (CH), 133.4 (CH), 130.4 (C), 129.8 (CH), 129.7 (CH), 129.4 (CH), 128.7 (CH), 128.5 (CH), 127.7 (CH), 83.3 (C), 60.5 (CH_2), 24.2 (CH_2). HRMS-FAB+ $[MH]^+$ Calc. for $C_{24}H_{23}O_6S_2$: 471.0936; found: 471.0949.

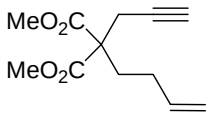
[259] Ashton, W. T.; Meurer, L. C.; Cantone, C. L.; Field, A. K. Hannah, J.; Karkas, J. D.; Liou, R.; Patel, G. F.; Perry, H. C. *J. Med. Chem.* **1988**, *31*, 2304-2315.

(*Z*)-5,5-Bis(phenylsulfonyl)oct-2-en-7-ynyl benzoate (1v)



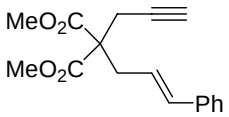
Starting from (*Z*)-5,5-Bis(phenylsulfonyl)pent-2-enyl benzoate (4.7 mmol) and propargyl bromide (80 % in tolene, 5.6 mmol) and following Procedure A for alkylations (DMF, 50 mL, 0ºC to 70 ºC, 22 h), **1v** was obtained in 41% yield as a yellowish sticky solid. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.08 (m, 6H), 7.56 (m, 9H), 5.99 (m, 2H), 4.87 (d, J = 6.3 Hz, 2H), 3.26 (s, 2H), 3.23 (d, J = 2.3 Hz, 2H), 2.07 (t, J = 2.3 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 166.6 (C), 136.6 (C), 135.3 (CH), 133.4 (CH), 131.9 (CH), 130.3 (C), 130.0 (CH), 129.1 (CH), 128.8 (CH), 128.6 (CH), 125.6 (CH), 88.7 (C), 75.9 (CH), 74.9 (CH), 61.1 (CH_2), 28.1 (CH_2), 21.2 (CH_2). HRMS-FAB+ $[M+Na]^+$ Calc. for $C_{27}H_{24}O_6S_2Na$: 531.0912; found: 531.0924.

Dimethyl 2-(but-3-enyl)-2-(prop-2-ynyl)malonate (5)



Starting from dimethyl propargylmalonate (5.876 mmol, Fluka) and 4-bromobut-1-ene (7.052 mmol, Aldrich), and following Procedure A for alkylations (THF, 10 mL, 0ºC to rt, 24 h), **5** was obtained in 45% yield as a colorless oil. Characterization and experimental data of the compound were already reported following other procedure.[274]

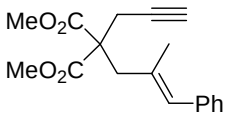
Dimethyl 2-cinnamyl-2-(prop-2-ynyl)malonate (8)



[274] Trost, B. M.; Ball, Z. T. *J. Am. Chem. Soc.* **2005**, *127*, 17644-17655.

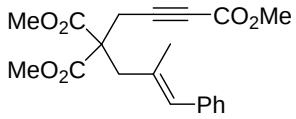
Starting from dimethyl propargylmalonate (5.876 mmol, Fluka) and (*E*)-(3-bromoprop-1-enyl)benzene or cinnamyl bromide (7.052 mmol, Aldrich), and following Procedure A for alkylations (THF, 10 mL, 0ºC to rt, 24 h), **8** was obtained in 67% yield as a colorless oil. Characterization and experimental data of the compound were already reported following other procedures.[153a,275]

(*E*)-Dimethyl 2-(2-methyl-3-phenylallyl)-2-(prop-2-ynyl)malonate (9)



Starting from dimethyl propargylmalonate (4.36 mmol, Fluka) and (*E*)-(3-chloro-2-methylprop-1-enyl)benzene[276] (4.8 mmol) and following Procedure A for alkylations (DMF, 50 mL, 0ºC to rt, 48 h), **9** was obtained in 59% yield as a colorless oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.16-7.99 (m, 5H), 7.26 (s, 1H), 4.57 (s, 6H), 3.82 (s, 2H), 3.71 (d, J = 2.3 Hz, 2H), 2.89 (t, J = 2.3 Hz, 1H), 2.60 (s, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 170.9, 138.0, 133.0, 131.2, 129.3, 128.4, 126.8, 79.5, 72.3, 57.4, 53.1, 43.0, 23.2, 19.0. HRMS-ESI+ $[MH]^+$ Calc. for $C_{18}H_{21}O_4$: 301.1434; found: 301.1438.

(*E*)-Trimethyl 6-methyl-7-phenylhept-6-en-1-yne-1,4,4-tricarboxylate (14)



Starting from enyne **11** (0.99 mmol) and methyl chloroformate (1.50 mmol, Aldrich) and following Procedure C (THF, 8 mL, 16 h), **14** was obtained in 78% yield as a pale yellowish oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.36-7.28 (m, 3H), 7.24-7.18 (m, 2H), 6.44 (s, 1H), 3.78 (s, 6H), 3.76 (s, 3H), 3.04 (s, 2H), 3.01 (s, 2H), 1.77 (s, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 170.2 (C), 153.9 (C), 137.7 (C), 132.4 (C), 131.5 (CH), 129.1 (CH), 128.3 (CH), 126.8 (CH), 84.2 (C), 75.9 (C), 56.9 (C), 53.2 (CH_3),

[153] (a) Chatani, N.; Morimoto, T.; Muto, T.; Murai, S. *J. Am. Chem. Soc.* **1994**, *116*, 6049-6050.
[275] Faller, J. W.; Fontaine, P. P. *J. Organomet. Chem.* **2006**, *691*, 1912-1918.
[276] Movassaghi, M.; Piizzi, G.; Siegel, D.S.; Pierstani, G. *Angew. Chem., Int. Ed.* **2006**, *45*, 5859-5863.

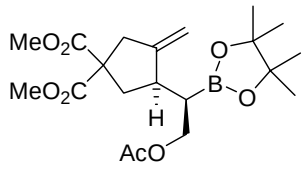
52.9 (CH_3), 43.3 (CH_2), 23.3 (CH_2), 18.8 (CH_3). HRMS-ESI+ $[MH]^+$ Calc. for $C_{20}H_{23}O_6$: 359.1489; found: 359.1482.

2.2 General optimized procedure for the synthesis of alkylboronates from enynes

The corresponding enyne (*ca.* 100 mg), bis(pinacolato)diboron (1.2 equiv), and $Pd(OAc)_2$ (5 mol%) were sequentially added to a 5 mL flask. After purging with Ar, dry toluene (2 mL) and MeOH (1 equiv) were added. The mixture was heated at 50ºC for the indicated time. After cooling to room temperature, Celite® was added and solvent was evaporated. Column chromatography (hexane-EtOAc) afforded the product. To obtain the highest possible yield, a 2 cm diameter column filled with 8.5 cm height of silicagel was used. Partial decomposition of the boronate was detected when using longer columns or retention times, probably due to hydrolysis, since boronates are stable in the presence of silicagel in dry toluene for 24 h at 23ºC. Using pinacol (50 mol %) instead of MeOH made chromatographic separation more difficult.

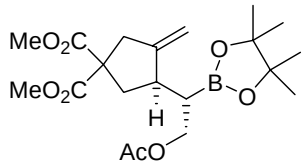
2.2.1 Experimental data of alkylboronates

(*rac*)-Dimethyl (3*R*)-3-[(1*R*)-2-(acetyloxy)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl]-4-methylenecyclopentane-1,1-dicarboxylate (2a)



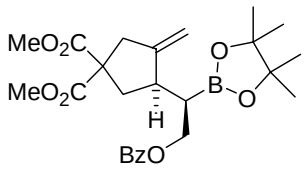
Following general borylative cyclization procedure, **2a** was obtained after 2.5 h in 59% yield as a colorless oil (hexane/EtOAc 9:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.94 (m, 1H), 4.83 (m, 1H), 4.16 (d, J = 7.8, 2H), 3.69 (s, 6H), 2.94 (m, 2H), 2.82-2.71 (m, 1H), 2.53 (dd, J = 12.7, 7.7 Hz, 1H), 2.17 (dd, J = 12.7, 10.7 Hz, 1H), 2.00 (s, 3H), 1.80-1.73 (m, 1H), 1.18 (s, 12H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.0 (C), 170.9 (C), 151.0 (C), 107.1 (CH_2), 83.4 (C), 64.8 (CH_2), 58.6 (C), 52.6 (CH_3), 41.0 (CH_2), 40.7 (CH), 38.0 (CH_2), 24.7 (CH), 24.6 (CH_3), 20.9 (CH_3). HRMS-FAB+ $[MH]^+$ Calc. for $C_{20}H_{33}BO_8$: 411.2190; found: 411.2171.

(*rac*)-Dimethyl (3*R*)-3-[(1*S*)-2-(acetyloxy)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl]-4-methylenecyclopentane-1,1-dicarboxylate (2a')



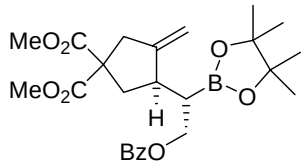
Starting from the isomeric enyne **(*E*)-1a** with (*E*) configuration on the alkene, the diastereoisomer **2a'** was obtained. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.93 (m, 1H), 4.88 (m, 1H), 4.21 (dd, J = 7.5, 4.2 Hz, 2H), 3.71 (s, 6H), 2.95 (m, 2H), 2.79 (m, 1H), 2.54 (m, 1H), 2.01 (m, 1H), 2.00 (s, 3H), 1.61 (m, 1H), 1.22 (s, 12H).

(*rac*)-Dimethyl (3*R*)-3-[(1*R*)-2-(benzoyloxy)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl]-4-methylenecyclopentane-1,1-dicarboxylate (2b)



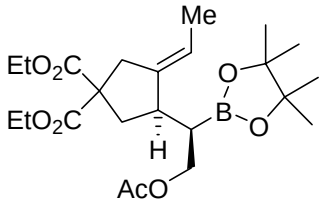
Following general borylative cyclization procedure, **2b** was obtained after 3 h in 76% yield as a crystalline white solid (hexane/EtOAc 7:1), mp 75-78 ºC. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.04 (m, 2H), 7.54 (m, 1H), 7.42 (m, 2H), 4.99 (d, J = 2.1 Hz, 1H), 4.90 (d, J = 2.1 Hz, 1H), 4.44 (m, 2H), 3.72 (s, 3H), 3.69 (s, 3H), 2.99 (s, 2H), 2.90 (m, 1H), 2.63 (dd, J = 7.7, 12.8 Hz, 1H), 2.29 (dd, J = 10.8, 12.8 Hz, 1H), 1.94 (c, J = 6.8 Hz, 1H), 1.19 (s, 12H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.6 (C), 172.4 (C), 166.8 (C), 151.5 (C), 133.2 (CH), 130.9 (C), 130.0 (CH), 128.6 (CH), 107.7 (CH_2), 83.9 (C), 65.8 (CH_2), 59.1 (C), 53.1 (CH_3), 53.0 (CH_3), 41.4 (CH), 41.4 (CH_2), 38.6 (CH_2), 28.7 (CH), 25.1 (CH_3). HRMS-ESI+ $[MH]^+$ Calc. for $C_{25}H_{34}BO_8$: 473.2341; found: 473.2362.

(*rac*)-Dimethyl (3*R*)-3-[(1*R*)-2-(benzoyloxy)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl]-4-methylenecyclopentane-1,1-dicarboxylate (2b')



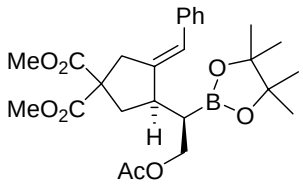
Starting from the isomeric enyne **(*E*)-1b** with (*E*) configuration on the alkene, the diastereoisomer **2b'** was obtained. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01 (m, 2H), 7.51 (m, 1H), 7.39 (m, 2H), 4.93 (m, 2H), 4.45 (dd, J = 7.0, 1.2 Hz, 2H), 3.68 (s, 3H), 3.67 (s, 3H), 2.97 (m, 2H), 2.88 (m, 1H), 2.61 (m, 1H), 2.05 (dd, J = 12.9, 11.6 Hz, 1H), 1.74 (c, J = 6.4 Hz, 1H), 1.19 (s, 6H), 1.18 (s, 6H).

(*E*)-Diethyl 3-(2-acetoxy-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)-4-ethylidenecyclopentane-1,1-dicarboxylate (2c)



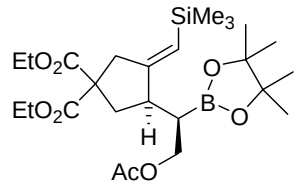
Following general borylative cyclization procedure, **2c** was obtained after 4 h in 95% yield as a colorless oil (hexane/EtOAc 9:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.25 (m, 1H), 4.22-4.11 (m, 4H), 2.97 (d, J = 16.3Hz, 1H), 2.75 (m, 2H), 2.47 (dd, J = 11.4, 6.7 Hz, 1H), 2.18 (dd, J = 11.4, 12.7 Hz, 1H), 1.99 (s, 3H), 1.81 (m, 1H), 1.57 (d, J = 6.7 Hz, 3H), 1.25-1.19 (m, 6H), 1.17 (s, 6H), 1.16 (s, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 171.9 (C), 171.0 (C), 142.1 (C), 116.5 (CH), 83.2 (C), 64.9 (CH_2), 61.3 (CH_2), 58.7 (C), 40.7 (CH), 37.6 (CH_2), 37.1 (CH_2), 24.7 (CH_3), 24.6 (CH), 20.9 (CH_3), 14.5 (CH_3), 14.0 (CH_3), 13.9 (CH_3). HRMS-FAB+ $[MH]^+$ Calc. for $C_{27}H_{38}BO_8$: 453.2659; found: 453.2652.

(*E*)-Dimethyl 3-(2-acetoxy-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)-4-benzylidenecyclopentane-1,1-dicarboxylate (2d)



Following general borylative cyclization procedure, **2d** was obtained after 3.5 h in 81% yield as a colorless oil (hexane/EtOAc 9:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.37-7.17 (m, 5H), 6.31 (m, 1H), 4.26 (d, J = 8.1 Hz, 2H), 3.77 (s, 3H), 3.70 (s, 3H), 3.34 (d, J = 16.7 Hz, 1H), 3.24 (dt, J = 16.7, 2.9 Hz, 1H), 3.10-3.01 (m, 1H), 2.59 (dd, J = 7.7, 13.1 Hz, 1H), 2.24 (m, 1H), 2.05 (s, 3H), 1.97 (m, 1H), 1.26 (s, 6H), 1.24 (s, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.2 (C), 172.1(C), 171.0 (C), 144.5 (C), 138.0 (C), 128.3 (CH), 128.2 (CH), 126.2 (CH), 122.9 (CH), 83.5 (C), 83.2 (C), 64.8 (CH_2), 59.5 (C), 59.8 (CH_3), 59.7 (CH_3), 42.6 (CH), 39.3 (CH_2), 37.2 (CH_2), 24.9 (CH_3), 24.8 (CH_3), 24.6 (CH), 21.0 (CH_3). HRMS-FAB+ $[MH]^+$ Calc. for $C_{26}H_{37}BO_8$: 487.2503; found: 487.2519.

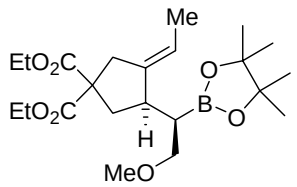
(*E*)-Diethyl 3-(2-acetoxy-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)-4-((trimethylsilyl)methylene)cyclopentane-1,1-dicarboxylate (2e)



Following general borylative cyclization procedure, **2e** was obtained after 50 h in 79% yield as a colorless oil (hexane/EtOAc 20:1). After 25 h, additional $Pd(OAc)_2$ (5 mol%) and MeOH (1 equiv) were added. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.33 (m, 1H), 4.16 (m, 6H), 3.05 (dm, J = 16.6 Hz, 1H), 2.9 (dt, J = 16.6, 2.6 Hz, 1H), 2.80-2.70 (m, 1H), 2.50 (ddd, J = 1.6, 7.7, 12.6 Hz, 1H), 2.24 (dd, J = 11.5, 12.6 Hz, 1H), 2.00 (s, 3H), 1.86 (m, 1H), 1.23 (dt, J = 3.9, 7.1 Hz, 6H), 1.18 (s, 6H), 1.17 (s, 6H), 0.07 (s, 9H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 171.7 (C), 171.0 (C), 160.4 (C), 149.5 (C), 119.9 (CH),

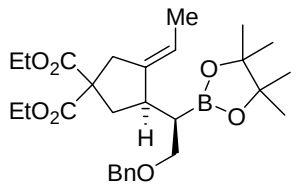
83.5 (C), 83.3 (C), 64.9 (CH_2), 61.4 (CH_2), 59.1 (C), 43.5 (CH), 40.6 (CH_2), 37.0 (CH_2), 27.7 (CH-B), 25.1 (CH_3), 24.9 (CH_3), 20.9 (CH_3), 14.0 (CH_3), -0.40 (CH_3). HRMS-ESI+ $[MH]^+$ Calc. for $C_{25}H_{44}BO_8Si$: 511.2893; found: 511.2904.

(*E*)-Diethyl 3-ethylidene-4-(2-methoxy-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)cyclopentane-1,1-dicarboxylate (2f)



Following general borylative cyclization procedure, **2f** was obtained after 24 h in 80% yield as a colorless oil (hexane/EtOAc 9:1). After 9 h, additional $Pd(OAc)_2$ (5 mol%) and MeOH (1 equiv) were added. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.26 (m, 1H), 4.24-4.11 (m, 4H), 3.46 (d, J = 7.6 Hz, 2H), 3.29 (s, 3H), 2.97 (d, J = 16.4 Hz, 1H), 2.76 (dm, J = 15.8 Hz, 2H), 2.48 (dd, J = 7.6, 11.4 Hz, 1H), 2.19 (dd, J = 11.4, 19.6 Hz, 1H), 1.79 (m, 1H), 1.56 (d, 3H),1.27-1.20 (m, 6H), 1.18 (s, 6H), 1.17 (s, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.1 (C), 172.0 (C), 142.7 (C), 116.1 (CH), 83.2 (C), 73.0 (CH_2), 61.3 (CH_2), 58.6 (CH_3), 58.2 (C), 40.7 (CH), 37.9 (CH_2), 37.2 (CH_2), 28.5 (CH), 24.9 (CH_3), 24.78 (CH_3), 14.5 (CH_3), 14.1 (CH_3), 14.0 (CH_3). HRMS-FAB+ $[MH]^+$ Calc. for $C_{22}H_{38}BO_7$: 425.2710; found: 425.2700.

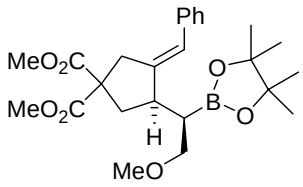
(*E*)-Diethyl 3-(2-(benzyloxy)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)-4-ethylidenecyclopentane-1,1-dicarboxylate (2g)



Following general borylative cyclization procedure, **2g** was obtained after 4 h in 93% yield as a colorless oil (hexane/EtOAc 9:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34-7.21 (m, 5H), 5.27 (m, 1H), 4.49 (d, J = 1.3 Hz, 2H), 4.17 (m, 4H), 3.57 (m, 2H), 2.98 (d, J =

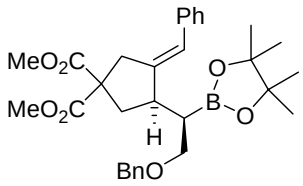
16.4 Hz, 1H), 2.80 (m, 1H), 2.75 (dm, J = 16.4 Hz, 1H), 2.48 (ddd, J = 12.6, 7.4, 1.6 Hz, 1H), 2.22 (dd, J = 12.6, 1.2 Hz, 1H), 1.80 (m, 1H), 1.57 (m, 3H), 1.23 (m, 6H), 1.17 (s, 6H), 1.16 (s, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.5 (C), 172.4 (C), 143.0 (C), 139.2 (C), 128.6 (CH), 127.8 (CH), 127.6 (CH), 116.5 (CH), 83.3 (C), 73.2 (CH_2), 71.1 (CH_2), 61.6 (CH_2), 59.2 (C), 41.1 (CH), 38.2 (CH_2), 37.6 (CH_2), 29.2 (CH), 25.2 (CH_3), 25.0 (CH_3), 14.8 (CH_3), 14.4 (CH_3). HRMS-FAB+ $[MH]^+$ Calc. for $C_{28}H_{42}BO_7$: 501.3023; found: 501.3038.

(*E*)-Dimethyl 3-benzylidene-4-(2-methoxy-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)cyclopentane-1,1-dicarboxylate (2h)



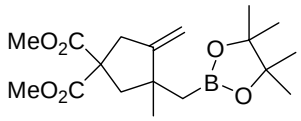
Following general borylative cyclization procedure, **2h** was obtained after 3 h in 77% yield as a colorless oil (hexane/EtOAc 18:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33-7.14 (m, 5H), 6.28 (d, J = 2.2 Hz, 1H), 3.74 (s, 3H), 3.66 (s, 3H), 3.53 (m, 2H), 3.32 (s, 3H), 3.28 (br s, 1H), 3.21 (dt, J = 17.1, 2.8 Hz, 1H), 3.04 (m, 1H), 2.58 (dd, J = 12.8, 7.4 Hz, 1H), 2.25 (dd, J = 12.8, 10.8 Hz, 1H), 1.90 (m, 1H), 1.17 (s, 6H), 1.16 (s, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.6 (C), 172.5 (C), 145.6 (C), 138.5 (C), 128.6 (CH), 128.5 (CH), 126.3 (CH), 122.8 (CH), 83.5 (C), 73.1 (CH_2), 59.9 (C), 58.9 (CH_3), 53.0 (CH_3), 52.9 (CH_3), 43.0 (CH), 39.5 (CH_2), 37.7 (CH_2), 29.8 (CH), 25.2 (CH_3), 24.9 (CH_3). HRMS-FAB+ $[MH]^+$ Calc. for $C_{25}H_{36}BO_7$: 459.2554; found: 459.2565.

(*E*)-Dimethyl 3-benzylidene-4-(2-(benzyloxy)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)cyclopentane-1,1-dicarboxylate (2i)



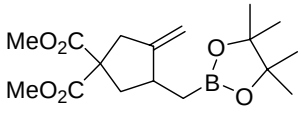
Following general borylative cyclization procedure, **2i** was obtained after 3 h in 71% yield as a colorless oil (hexane/EtOAc 20:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34-7.10 (m, 10H), 6.26 (d, J = 2.5, 1H), 4.49 (m, 2H), 3.71 (s, 3H), 3.65 (s, 3H), 3.62 (m, 2H), 3.29 (d, J = 17.2 Hz, 1H), 3.17 (dt, J = 17.2, 2.8 Hz, 1H), 3.08 (m, 1H), 2.55 (ddd, J = 12.8, 7.6, 1.3 Hz, 1H), 2.25 (dd, J = 12.8, 10.8 Hz, 1H), 1.96 (m, 1H), 1.13 (s, 6H), 1.12 (s, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.6 (C), 172.5 (C), 145.5 (C), 139.2 (C), 138.6 (C), 128.7 (CH), 128.6 (CH), 128.5 (CH), 127.9 (CH), 127.7 (CH), 126.4 (CH), 122.9 (CH), 83.6 (C), 73.3 (CH_2), 70.8 (CH_2), 59.9 (C), 53.1 (CH_3), 53.0 (CH_3), 43.1 (CH), 39.7 (CH_2), 37.8 (CH_2), 29.7 (CH), 25.3 (CH_3), 25.0 (CH_3). HRMS-FAB+ $[MH]^+$ Calc. for $C_{31}H_{40}BO_7$: 535.2867; found: 535.2879.

Dimethyl 3-methyl-4-methylene-3-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)cyclopentane-1,1-dicarboxylate (2j)



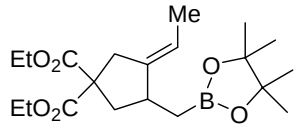
Following general borylative cyclization procedure, **2j** was obtained after 3 h in 75% yield as a colorless oil (hexane/EtOAc 10:1). It contains traces of cyclopropyl derivatives type of **12** or **13** (98:2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.80 (m, 1H), 4.76 (m, 1H), 3.70 (s, 3H), 3.69 (s, 3H), 3.06 (m, 2H), 2.48 (d, J = 13.8 Hz, 1H), 2.32 (d, J = 13.8 Hz, 1H), 1.20 (s, 12H), 1.10 (s, 3H), 0.98 (d, J = 4.6 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.9 (C), 172.7 (C), 159.0 (C), 104.5 (CH_2), 83.1 (C), 82.9 (C), 57.7 (C), 52.8 (CH_3), 52.7 (CH_3), 47.9 (CH_2), 40.8 (CH_2), 38.1 (CH), 29.2 (CH_3), 24.9 (CH_3), 24.8 (CH_3). HRMS-ESI+ $[MH]^+$ Calc. for $C_{18}H_{30}BO_6$: 353.2129; found: 353.2133.

Dimethyl 3-methylene-4-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)cyclopentane-1,1-dicarboxylate (2k)



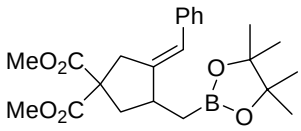
Following general borylative cyclization procedure, **2k** was obtained after 3.5 h in 78% yield as a colorless oil (hexane/EtOAc 9:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.87 (m, 1H), 4.82 (m, 1H), 3.72 (s, 3H), 3.71 (s, 3H), 3.04 (dm, J = 16.9 Hz, 1H), 2.94 (dm, J = 16.9 Hz, 1H), 2.74-2.57 (m, 2H), 1.84 (dd, J = 10.3, 11.9 Hz, 1H), 1.24 (s, 12H), 1.08 (dd, J = 5.6, 15.7 Hz, 1H), 0.87 (dd, J = 7.7, 15.7 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.5 (C), 172.4 (C), 153.6 (C), 105.6 (CH_2), 83.1 (C), 58.2 (C), 52.7 (CH_3), 52.6 (CH_3), 42.0 (CH_2), 40.6 (CH_2), 38.7 (CH), 24.9 (CH_3), 24.8 (CH_3), 15.7 (CH). HRMS-FAB+ $[MH]^+$ Calc. for $C_{17}H_{28}BO_6$: 339.1978; found: 339.1986.

(*E*)-Diethyl 3-ethylidene-4-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)cyclopentane-1,1-dicarboxylate (2l)



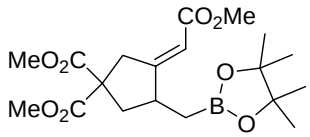
Following general borylative cyclization procedure, **2l** was obtained after 6 h in 93% yield as a colorless oil (hexane/EtOAc 9:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.18 (m, 1H), 4.16 (m, 4H), 2.96 (dm, J = 17.1 Hz, 1H), 2.79 (dm, J =17.1 Hz, 1H), 2.60 (m, 1H), 2.54 (ddd, J = 12.1, 7.1, 1.5 Hz, 1H), 1.78 (dd, J = 12.1, 11.0 Hz, 1H), 1.56 (dm, J = 6.8 Hz, 3H), 1.22 (t, J = 7.6 Hz, 6H), 1.21 (s, 6H), 1.20 (s, 6H), 1.03 (dd, J = 15.6, 5.4 Hz, 1H), 0.80 (dd, J = 15.6, 7.8 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.6 (C), 172.4 (C), 144.8 (C), 115.2 (CH), 83.4 (C), 61.7 (CH_2), 61.6 (CH_2), 58.7 (C), 42.3 (CH_2), 38.9 (CH), 37.2 (CH_2), 25.2 (CH_3), 25.0 (CH_3), 15.6 (CH_2), 14.8 (CH_3), 14.4 (CH_3). HRMS-FAB+ $[MH]^+$ Calc. for $C_{20}H_{34}BO_6$: 381.2448; found: 381.2433.

(*E*)-Dimethyl 3-benzylidene-4-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)cyclopentane-1,1-dicarboxylate (2m)



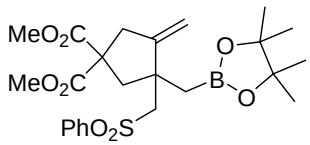
Following general borylative cyclization procedure, **2m** was obtained after 70 h in 86% yield as a colorless oil (hexane/EtOAc 9:1). After 23 h, additional $Pd(OAc)_2$ (5 mol%) and MeOH (1 equiv) were added. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28 (m, 4H), 7.15 (m, 1H), 6.23 (d, J = 2.5 Hz, 1H), 3.70 (s, 3H), 3.69 (s, 3H), 3.34 (d, J = 17.5 Hz, 1H), 3.19 (dt, J = 17.5, 2.5 Hz, 1H), 2.88 (m, 1H), 2.63 (ddd, J = 12.7, 7.2, 1.4 Hz, 1H), 1.87 (dd, J = 12.7, 11.6 Hz, 1H), 1.22 (s, 6H), 1.21 (s, 6H), 1.18 (dd, J = 15.7, 5.8 Hz, 1H), 0.99 (dd, J = 15.7, 7.7 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.7 (C), 172.6 (C), 147.0 (C), 138.4 (C), 128.7 (CH), 128.6 (CH), 126.5 (CH), 121.9 (CH), 83.5 (C), 59.4 (C), 53.1 (CH_3), 53.0 (CH_3), 41.5 (CH_2), 40.8 (CH), 39.3 (CH_2), 25.3 (CH_3), 25.1 (CH_3), 16.0 (CH_2). HRMS-FAB+ $[MH]^+$ Calc. for $C_{23}H_{32}BO_6$: 414.2213; found: 414.2227.

(*E*)-Dimethyl 3-(2-methoxy-2-oxoethylidene)-4-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)cyclopentane-1,1-dicarboxylate (2n)



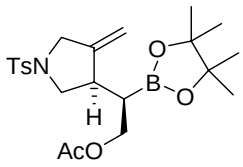
Following general borylative cyclization procedure, **2n** was obtained after 4.5 h in 43% yield as a colorless oil (hexane/EtOAc 5:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.70 (c, J = 2.4 Hz, 1H), 3.72 (s, 3H), 3.71 (s, 3H), 3.68 (s, 3H), 3.66 (dt, J = 19.8, 2.0 Hz, 1H), 3.34 (dt, J = 19.8, 2.5 Hz, 1H), 2.84 (m, 1H), 2.62 (ddd, J = 12.7, 7.4, 1.8 Hz, 1H), 1.90 (t, J = 12.3 Hz, 1H), 1.23 (s, 6H), 1.22 (s, 6H), 1.12 (dd, J = 15.9, 5.6 Hz, 1H), 0.90 (dd, J = 15.9, 8.1 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.2 (C), 172.0 (C), 168.4 (C), 167.3 (C), 112.1 (CH), 83.6 (C), 58.7 (C), 53.0 (CH_3), 52.9 (CH_3), 51.2 (CH_3), 41.0 (CH), 40.9 (CH_2), 40.6 (CH_2), 25.0 (CH_3), 24.9 (CH_3), 15.2 (CH_2-B). HRMS-ESI+ $[M+NH_4]^+$ Calc. for $C_{19}H_{33}BNO_8$: 414.2293; found: 414.2293.

Dimethyl 4-methylene-3-(phenylsulfonylmethyl)-3-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)cyclopentane-1,1-dicarboxylate (2o)



Following general borylative cyclization procedure, **2o** was obtained after 5 h in 31% yield as a colorless oil (hexane/EtOAc 5:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91 (m, 2H), 7.61 (m, 1H), 7.53 (m, 2H), 4.90 (m, 2H), 3.72 (d, J =14.0 Hz, 1H), 3.72 (s, 3H), 3.71 (s, 3H), 3.29 (d, J =14.0 Hz, 1H), 3.12 (dt, J =16.8, 1.9 Hz, 1H), 3.06 (d, J = 14.5 Hz, 1H), 2.94 (dm, J =16.8 Hz, 1H), 2.56 (d, J = 14.5 Hz, 1H), 1.50 (d, J =16.4 Hz, 1H), 1.44 (d, J =16.4 Hz, 1H), 1.23 (s, 6H), 1.22 (s, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 173.3 (C), 172.4 (C), 155.6 (C), 142.3 (C), 133.7 (CH), 129.4 (CH), 128.1 (CH), 108.5 (CH_2), 83.6 (C), 63.5 (CH_2), 57.8 (C), 53.3 (CH_3), 53.2 (CH_3), 46.1 (CH_2), 46.0 (C), 40.5 (CH_2), 25.3 (CH_3), 25.1 (CH_3), 23.3 (CH_2). HRMS-FAB+ $[MH]^+$ Calc. for $C_{24}H_{34}BO_8S$: 493.2067; found: 493.2068.

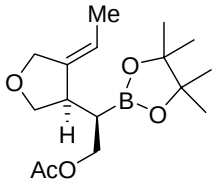
2-(4-Methylene-1-tosylpyrrolidin-3-yl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl acetate (2r)



Following general borylative cyclization procedure, **2r** was obtained after 2.5 h in 30% yield as a colorless oil (hexane/EtOAc 5:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71 (d, J = 8.2 Hz, 2H), 7.32 (d, J = 8.2 Hz, 2H), 4.93 (dd, J = 4.3, 2.2 Hz, 1H), 4.87 (dd, J = 4.6, 2.2 Hz, 1H), 4.12 (d, J = 1.2 Hz, 1H), 4.09 (s, 1H), 3.92 (dt, J = 13.8 Hz, 1H), 3.65 (ddd, J = 13.8, 4.3, 2.2 Hz, 1H), 3.50 (dd, J = 9.3, 7.8 Hz, 1H), 3.15, dd, J = 9.3, 7.8 Hz, 1H), 2.86 (m, 1H), 2.41 (s, 3H), 1.99 (s, 3H), 1.66 (dd, J = 13.2, 6.4 Hz, 1H), 1.08 (s, 6H), 1.06 (s, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 171.2 (C), 147.7 (C), 143.8 (C), 132.9 (C), 129.9 (CH), 128.4 (CH), 107.6 (CH_2), 83.9(C), 64.7 (CH_2), 52.7 (CH_2),

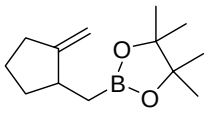
52.6 (CH_2), 41.6 (CH), 25.0 (CH), 24.8 (CH_3), 21.9 (CH_3), 21.2 (CH_3). HRMS-ESI+ $[MH]^+$ Calc. for $C_{22}H_{33}BNO_6S$: 450.2116; found: 450.2115.

(*Z*)-2-(4-Ethylidene-tetrahydrofuran-3-yl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl acetate (2s)



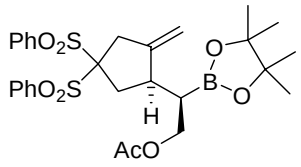
Following general borylative cyclization procedure, **2s** was obtained after 84 h in 21% yield (Conv.: 68%, 31% yield corrected for this rate of conversion) as a colorless oil (hexane/EtOAc 9:1). After 21 h, additional $Pd(OAc)_2$ (5 mol%) was added. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.31 (m, 1H), 4.29 (m, 2H), 4.25-4.10 (m, 2H), 3.90 (dd, J = 6.3, 8.3 Hz 1H), 3.80 (dd, J = 6.0, 8.3 Hz 1H), 2.81 (m, 1H), 2.02 (s, 3H), 1.68-1.61 (m, 1H), 1.56 (dm, J = 7.0 Hz, 3H), 1.20 (s, 12H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 171.0 (C), 142.3 (C), 114.9 (CH), 83.5 (C), 83.4 (C), 72.7 (CH_2), 69.1 (CH_2), 64.9 (CH_2), 42.4 (CH), 25.0 (CH), 24.8 (CH_3), 24.7 (CH_3), 20.9 (CH_3), 14.6 (CH_3). HRMS-FAB+ $[MH]^+$ Calc. for $C_{16}H_{28}BO_5$: 311.2029; found: 311.2027.

4,4,5,5-Tetramethyl-2-((2-methylenecyclopentyl)methyl)-1,3,2-dioxaborolane (2t)



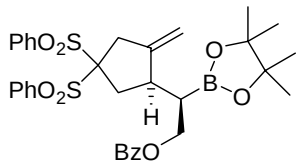
Following general borylative cyclization procedure, **2t** was obtained after 20 h in 14% yield as a colorless oil (hexane/EtOAc 12:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.82 (s, 1H), 4.78 (s, 1H), 2.50 (m, 1H), 2.38-2.27 (m, 2H), 1.94 (m, 1H), 1.69 (m, 1H), 1.59-1.44 (m, 1H), 1.25 (s, 13H), 1.10 (dd, J = 15.6, 5.6 Hz, 1H), 0.81 (dd, J = 15.6, 9.1 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 158.7 (C), 103.7 (CH_2), 83.1 (C), 40.3 (CH), 35.4 (CH_2), 32.8 (CH_2), 25.1 (CH_3), 24.9 (CH_3), 24.0 (CH_2), 16.4 (CH_2-B).

2-(2-Methylene-4,4-bis(phenylsulfonyl)cyclopentyl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl acetate (2u)



Following general borylative cyclization procedure, **2u** was obtained after 3 h in 47% yield as a sticky white solid (hexane/EtOAc 5:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.10 (m, 2H), 8.04 (m, 2H), 7.70 (m, 2H), 7.58 (m, 4H), 4.95 (d, J = 2.2 Hz, 1H), 4.90 (d, J = 2.2 Hz, 1H), 4.13 (m, 2H), 3.50 (dd, J = 18.0. 2.0 Hz, 1H), 3.05 (d, J = 18.0 Hz, 1H), 2.96 (m, 1H), 2.89 (m, 1H), 2.56 (dd, J = 14.3, 7.6 Hz, 1H), 2.01 (s, 3H), 1.84 (dd, J = 12.8, 6.6 Hz), 1.25 (s, 6H), 1.24 (s, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 171.2 (C), 149.3 (C), 137.5 (C), 136.3 (C), 134.9 (CH), 134.7 (CH), 131.7 (CH), 131.6 (CH), 129.0 (CH), 128.8 (CH), 108.1 (CH_2), 91.9 (C), 84.1 (C), 65.1 (CH_2), 42.1 (CH), 38.4 (CH_2), 36.0 (CH_2), 27.3 (CH), 25.1 (CH_3), 25.0 (CH_3), 21.3 (CH_3). HRMS-FAB+ $[MH]^+$ Calc. for $C_{28}H_{36}BO_8S_2$: 575.1944; found: 575.1963.

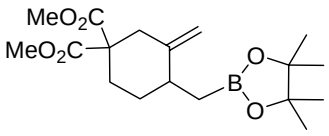
2-(2-Methylene-4,4-bis(phenylsulfonyl)cyclopentyl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl benzoate (2v)



Following general borylative cyclization procedure, **2v** was obtained after 5 h in 47% yield as a sticky white solid (hexane/EtOAc 9:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.09 (m, 2H), 8.02 (m, 4H), 7.65 (m, 2H), 7.55 (m, 3H), 7.46 (m, 4H), 4.98 (d, J = 2.2 Hz, 1H), 4.95 (d, J = 2.2 Hz, 1H), 4.38 (m, 2H), 3.53 (dd, J = 18.0, 2.0 Hz, 1H), 3.10 (d, J = 18.0 Hz, 1H), 3.06 (m, 1H), 3.00 (m, 1H), 2.62 (dd, J =14.0, 7.4 Hz, 1H), 2.01 (dd, J = 13.2, 6.2 Hz, 1H), 1.25 (s, 12H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 166.8 (C), 149.4 (C), 137.5 (C), 136.3 (C), 134.9 (CH), 134.7 (CH), 133.4 (CH), 131.7 (CH), 131.6 (CH), 130.6 (C), 130.0 (CH), 129.0 (CH), 128.9 (CH), 128.8 (CH), 108.2 (CH_2),

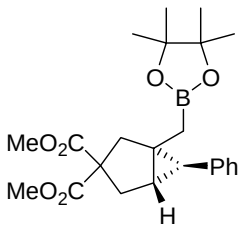
91.9 (C), 84.2 (C), 65.7 (CH_2), 42.3 (CH), 38.5 (CH_2), 35.9 (CH_2), 25.2 (CH_3), 25.1 (CH_3), 21.4 (CH). HRMS-FAB+ $[MH]^+$ Calc. for $C_{33}H_{38}BO_8S_2$: 637.2101; found: 637.2104.

Dimethyl 3-methylene-4-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)cyclohexane-1,1-dicarboxylate (6)



Following general borylative cyclization procedure, **6** was obtained after 65 h in 27% yield as a sticky white solid (hexane/EtOAc 9:1). After 21 h, additional $Pd(OAc)_2$ (5 mol%) was added. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.75 (m, 1H), 4.72 (m, 1H), 3.69 (s, 3H), 3.68 (s, 3H), 2.90 (dd, J = 13.4, 1.9 Hz, 1H), 2.55 (d, J = 13.4 Hz, 1H), 2.36-2.23 (m, 2H), 1.93-1.78 (m, 2H), 1.42-1.27 (m, 1H), 1.22 (s, 12H), 1.03 (dd, J = 6.6, 15.4 Hz, 1H), 0.80 (dd, J = 7.5, 15.4 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.2 (C), 171.1 (C), 148.5 (C), 108.7 (CH_2), 83.5 (C), 83.0 (C), 57.2 (C), 52.6 (CH_3), 52.3 (CH_3), 40.1 (CH_2), 38.2 (CH), 32.9 (CH_2), 30.7 (CH_2), 24.8 (CH_3), 24.8 (CH_3). HRMS-ESI+ $[MH]^+$ Calc. for $C_{18}H_{30}BO_6$: 353.2129; found: 353.2127.

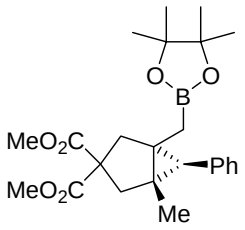
Dimethyl 6-phenyl-1-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)bicyclo[3.1.0]hexane-3,3-dicarboxylate (10)



Following general borylative cyclization procedure, cyclopropyl derivative **10** was obtained after 8 h in 36% yield as a sticky white solid (hexane/EtOAc 12:1). It was obtained along with traces (93:7) of a different compound which seems to be the corresponding alkylboronate of the general structure type of **2**. ^{1}H NMR (300 MHz,

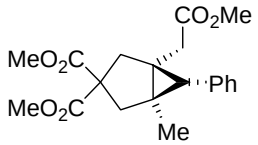
$CDCl_3$) δ 7.23-7.08 (m, 6H), 3.74 (s, 3H), 3.70 (s, 3H), 2.86 (d, J = 13.9 Hz, 1H), 2.74 (dd, J = 13.9, 5.1 Hz, 1H), 2.66 (d, J = 13.5 Hz, 1H), 2.47 (d, J = 14.0 Hz, 1H), 1.73 (d, J = 4.2 Hz, 1H), 1.66 (m, 1H), 1.18 (s, 6H), 1.17 (s, 6H), 0.74 (m, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 173.5 (C), 172.7(C), 139.0 (C), 129.0 (CH), 127.9 (CH), 125.6 (CH), 83.0 (C), 60.7 (C), 52.9 (CH_3), 52.8 (CH_3), 43.6 (CH_2), 37.4 (CH_2), 33.8 (C), 31.9 (CH), 29.1 (CH), 25.0 (CH_3), 24.9 (CH_3), 14.1 (CH_2). HRMS-ESI+ $[MH]^+$ Calc. for $C_{23}H_{32}BO_6$: 415.2286; found: 415.2303.

Dimethyl 1-methyl-6-phenyl-5-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)bicyclo[3.1.0]hexane-3,3-dicarboxylate (11)



Following general borylative cyclization procedure, cyclopropyl derivative **11** was obtained after 30 h in 30% yield as a sticky white solid (hexane/EtOAc 15:1). After 8 h, additional $Pd(OAc)_2$ (5 mol%) and MeOH (1 equiv) were added. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24-7.02 (m, 5H), 3.62 (s, 3H), 3.61 (s, 3H), 2.83 (d, J =13.7 Hz, 1H), 2.77 (d, J = 13.6 Hz, 1H), 2.47 (d, J =13.7 Hz, 1H), 2.38 (d, J =13.6 Hz, 1H), 1.56 (s, 1H), 1.16 (s, 12H), 0.96 (s, 3H), 0.81 (d, J = 16.5 Hz, 1H), 0.59 (d, J = 16.5 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 173.9 (C), 173.1 (C), 138.3 (C), 131.6 (CH), 128.2 (CH), 126.0 (CH), 83.8 (C), 83.5 (C), 59.1 (C), 53.1 (CH_3), 53.0 (CH_3), 45.3 (CH_2), 44.4 (CH_2), 33.1 (C), 32.2 (CH), 31.9 (C), 25.4 (CH_3), 25.2 (CH_3), 15.7 (CH_3), 11.8 (CH_2). HRMS-FAB+ $[M]^+$ Calc. for $C_{24}H_{33}BO_6$: 428.2370; found: 428.2366.

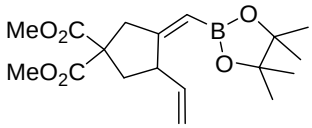
Dimethyl 1-(2-methoxy-2-oxoethyl)-5-methyl-6-phenylbicyclo[3.1.0]hexane-3,3-dicarboxylate (15)



Following general borylative cyclization procedure, non-borylated cyclopropyl derivative **15** was obtained after 21 h in 27% yield as a crystalline white solid (hexane/EtOAc 6:1), mp 110-115 ºC. Additional 17% yield was obtained from the corresponding alkylboronate of the general structure type of **2**. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30-7.12 (m, 5H), 3.72 (s, 6H), 3.69 (s, 3H), 2.90 (d, J = 14.4 Hz, 2H), 2.67 (d, J = 13.9 Hz, 1H), 2.51 (d, J = 11.3 Hz, 1H), 2.46 (d, J = 14.6 Hz, 1H), 2.25 (d, J = 17.3 Hz, 1H), 1.84 (s, 1H), 1.10 (s, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 173.3 (C), 172.9 (C), 172.6 (C), 136.9 (C), 131.1 (CH), 128.4 (CH), 126.4 (CH), 59.2 (C), 53.2 (CH_3), 53.0 (CH_3), 51.8 (CH_3), 44.9 (CH_2), 42.5 (CH_2), 34.5 (CH_2), 32.9 (CH), 32.4 (C), 32.1 (C), 15.7 (CH_3). HRMS-ESI+ $[MH]^+$ Calc. for $C_{20}H_{25}O_6$: 361.1645; found: 361.1635.

2.3 Synthesis of alkenylboronates

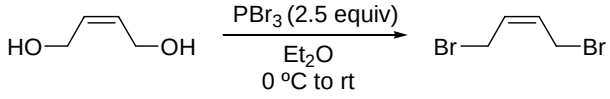
(*Z*)-Dimethyl 3-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methylene)-4-vinylcyclopentane-1,1-dicarboxylate (21)



Enyne **1a** (*ca.* 60 mg, 0.211 mmol), bis(pinacolato)diboron (0.253 mmol, 1.2 equiv), and $[Rh(cod)Cl]_2$ (0.011 mmol, 5 mol%) were sequentially added to a 5 mL flask. After purging with Ar, dry toluene (2 mL) was added. The mixture was heated at 50ºC for 48 h. After cooling to room temperature, Celite® was added and solvent was evaporated. Column chromatography (hexane/EtOAc 9:1) afforded the product **21** as a colorless oil in 30% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.80 (ddd, J = 6.2, 10.3, 17.2 Hz, 1H), 5.38 (m, 1H), 5.01 (dt, J = 1.6, 17.2 Hz, 1H), 4.92 (dt, J = 1.8, 10.3 Hz, 1H), 2.85 (m, 1H), 3.71 (s, 3H), 3.70 (s, 3H), 3.24 (dt, J = 1.9, 17 Hz, 1H), 2.85 (d, J = 17 Hz, 1H), 2.67 (ddd, J = 0.8, 8.5, 13.6 Hz, 1H), 2.27 (dd, J = 9.9, 13.6 Hz, 1H), 1.22 (s, 6H), 1.21 (s, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.10 (C), 172.06 (C), 165.58 (C), 140.50 (CH), 113.64 (CH_2), 82.91 (C), 58.41 (C), 52.83 (CH_3), 52.75 (CH_3), 45.72 (CH), 43.74 (CH_2), 39.36 (CH_2), 24.94 (CH_3), 24.78 (CH_3). HRMS-FAB+ $[MH]^+$ Calc. for $C_{18}H_{28}BO_6$: 351.1978; found: 351.1984.

3. Pd-Catalyzed Borylative Bicyclization of 6-Ene-1,11-diynes to Allylboronates

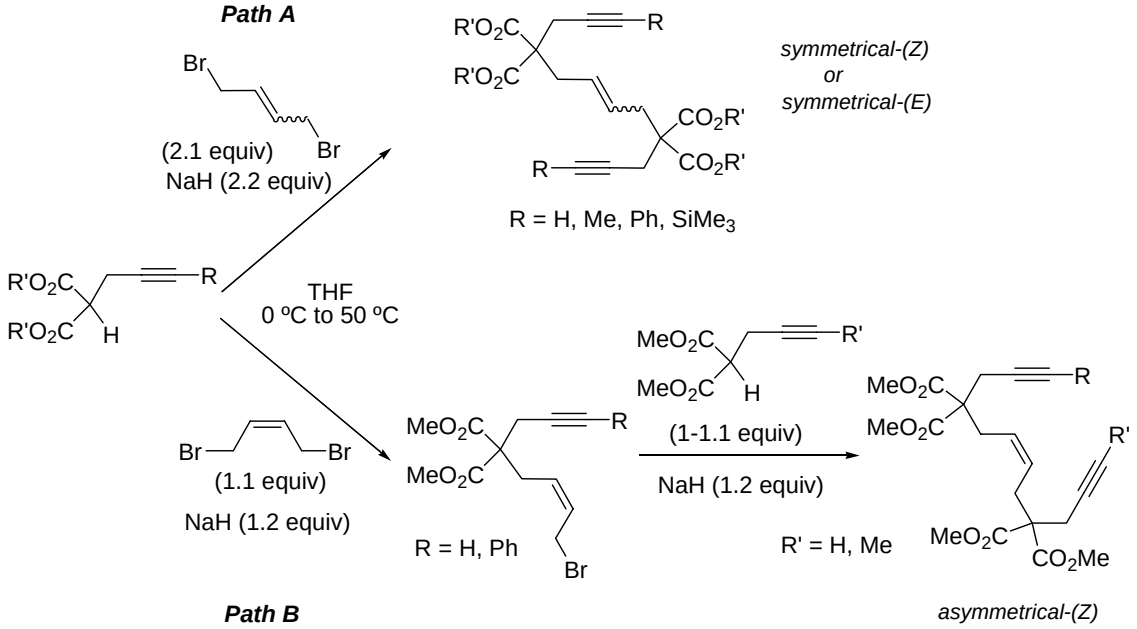
Two dibromide isomers were used as linkers between the malonate moieties in the preparation of 6-ene-1, 11-diynes. (*E*)-Dibromo-2-butene was purchased (Aldrich), and (*Z*)-dibromo-2-butene was prepared following next procedure:



To a solution of (*Z*)-butenediol (1.0 g, 11.35 mmol) in anhydrous Et_2O (15 mL) at 0 ºC was added dropwise PBr_3 (2.70 mL, 28.38 mmol) for 10 min. After addition the mixture was stirred at 0 ºC for 30 min. and then was warmed to rt for 3 h. Next, a solution of $NaHCO_3$ (5%) was added carefully at 0 ºC until the initial orange solution turned to colorless. Extractive work-up with Et_2O, drying over $MgSO_4$, filtration, and finally evaporation of the solvent afforded the dibromide compound (2.2 g, 10.30 mmol) without further purification (91% yield).

3.1 Preparation and experimental data of 6-ene-1,11-diynes

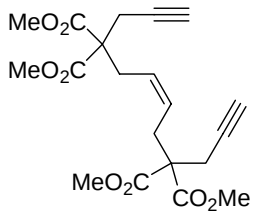
Both symmetrical and asymmterical 6-ene-1,11-diynes were prepared following the next reaction scheme and procedure:



General procedure for alkylation of malonate derivatives: To a suspension of NaH (60% in mineral oil, 2.2 equiv (*Path A*) or 1.2 equiv (*Path B*)) in anhydrous THF (volume will be indicated in each case) under Ar atmosphere at 0 ºC, was slowly added the corresponding malonate nucleophile (1 equiv) and the mixture was stirred at rt for 5-10 min. (formation of H_2 bubbles were observed during the addition). Then, the corresponding electrophile (2.1 equiv (*Path A*) or 1-1.1 equiv (*Path B*)) was added dropwise and the mixture was heated at 50 ºC (time will be specified in each case). Screening by TLC indicated the completion of the reaction. Then, most of the solvent was removed under vacuum and later, water and Et_2O were added into the resulting mixture. The aqueous layer was separated and extracted successively with Et_2O. The combined organic phases were dried over anhydrous Mg_2SO_4 and filtered through anhydrous Na_2SO_4. The solvent was removed under vacuum and the residue was purified by column chromatography (hexane/EtOAc).

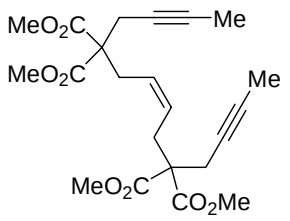
In the case of asymmetrical substrates to consecutive reactions under *Path B* conditions were neccessary due to the preparation of allylbromide malonate derivative intermediate.

(*Z*)-Tetramethyl dodeca-6-en-1,11-diyne-4,4,9,9-tetracarboxylate ((*Z*)-25a)



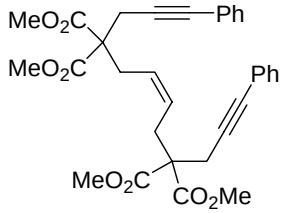
Starting from dimethyl propargylmalonate (5.24 mmol, Fluka) and (*Z*)-dibromo-2-butene (2.34 mmol) and following Path A for alkylations (THF, 15 mL, 0ºC to 50ºC, 70 h), **(*Z*)-25a** was obtained in 67% yield as a crystalline white solid (mp 73-75 ºC). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.38 (m, 2H), 3.73 (s, 12H), 2.86 (d, J = 6.0 Hz, 4H), 2.76 (d, J = 2.8 Hz, 4H), 2.03 (t, J = 2.8 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$, DEPT-135) δ 170.3 (C), 127.4 (CH), 78.9 (C), 71.8 (CH), 56.9 (C), 52.9 (CH_3), 30.2 (CH_2), 22.9 (CH_2). HRMS-FAB+ $[MH]^+$ Calc. for $C_{20}H_{25}O_8$: 393.1549; found: 393.1549.

(*Z*)-Tetramethyl tetradeca-7-en-2,12-diyne-5,5,10,10-tetracarboxylate ((*Z*)-25b)



Starting from dimethyl 2-(but-2-ynyl)malonate[272] (2.45 mmol) and (*Z*)-dibromo-2-butene (1.17 mmol) and following Path A for alkylations (THF, 8 mL, 0ºC to 50ºC, 65 h), **(*Z*)-25b** was obtained in 76% yield as a crystalline white solid (mp 80-82 ºC). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.37 (m, 2H), 3.73 (s, 12H), 2.87 (d, J = 5.9 Hz, 4H), 2.72 (c, J = 2.5 Hz, 4H), 1.78 (t, J = 2.5 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$, DEPT-135) δ 170.7 (C), 127.5 (CH), 79.4 (C), 73.5 (C), 57.2 (C), 52.9 (CH_3), 30.2 (CH_2), 23.2 (CH_2), 3.7 (CH_3). HRMS-FAB+ $[MH]^+$ Calc. for $C_{22}H_{29}O_8$: 421.1862; found: 421.1880.

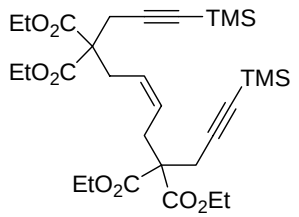
(*Z*)-Tetramethyl 1,12-diphenyldodeca-6-en-1,11-diyne-4,4,9,9-tetracarboxylate ((*Z*)-25c)



Starting from dimethyl 2-(3-phenylprop-2-ynyl)malonate[261] (2.45 mmol) and (*Z*)-dibromo-2-butene (1.17 mmol) and following Path A for alkylations (THF, 8 mL, 0ºC to 50ºC, 48 h), **(*Z*)-25c** was obtained in 77% yield as a crystalline white solid (mp 97-99 ºC). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40-7.33 (m, 4H), 7.30-7.20 (m, 6H), 5.49 (m, 2H), 3.73 (s, 12H), 3.03-2.96 (m, 8H). ^{13}C NMR (75 MHz, $CDCl_3$, DEPT-135) δ 170.5 (C), 131.1 (CH), 128.3 (CH), 128.2 (CH), 127.6 (CH), 123.3 (C), 84.4 (C), 83.9 (C), 57.4 (C), 52.9 (CH_3), 30.4 (CH_2), 23.9 (CH_2). HRMS-FAB+ $[MH]^+$ Calc. for $C_{32}H_{33}O_8$: 545.2175; found: 545.2202.

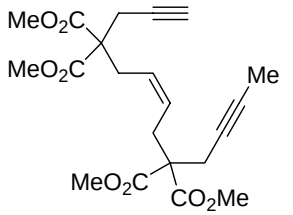
[261] Schiller, R.; Pour, M.; Fakova, H.; Kunes, J.; Cisarova, I. *J. Org. Chem.* **2004**, *69*, 6761-6765.
[272] Zhang, Q.; Xu, W.; Lu, X. *J. Org. Chem.* **2005**, *70*, 1505-1507.

(*Z*)-Tetraethyl 1,12-bis(trimethylsilyl)dodeca-6-en-1,11-diyne-4,4,9,9-tetracarboxylate ((*Z*)-25d)



Starting from diethyl 2-(3-(trimethylsilyl)prop-2-ynyl)malonate[262] (3.09 mmol) and (*Z*)-dibromo-2-butene (1.40 mmol) and following Path A for alkylations (THF, 10 mL, 0ºC to 50ºC, 23 h), **(*Z*)-25d** was obtained in 92% yield as a yellowish oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.41 (m, 2H), 4.19 (m, 8H), 2.83 (d, J = 5.9 Hz, 4H), 2.79 (s, 4H), 1.26 (t, J = 6.9 Hz, 12H), 0.14 (s, 18H). ^{13}C NMR (75 MHz, $CDCl_3$, DEPT-135) δ 169.9 (C), 127.5 (CH), 101.5 (C), 88.3 (C), 61.8 (CH_2), 57.2 (C), 30.0 (CH_2), 24.2 (CH_2), 14.2 (CH_3), 0.1 (CH_3). HRMS-FAB+ $[MH]^+$ Calc. for $C_{30}H_{49}O_8Si_2$: 593.2966; found: 593.2960.

(*Z*)-Tetramethyl trideca-6-en-1,11-diyne-4,4,9,9-tetracarboxylate ((*Z*)-25e)

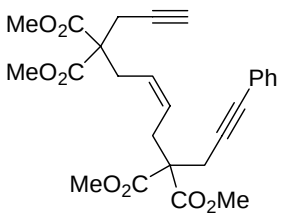


Starting from diethyl 2-(but-2-ynyl)malonate[272] (0.99 mmol) and (*Z*)-dimethyl 2-(4-bromobut-2-enyl)-2-(prop-2-ynyl)malonate[277] (R = H in the intermediate of *Path B*, 0.82 mmol) and following Path B for alkylations (THF, 9 mL, 0ºC to 50ºC, 15 h), **(*Z*)-25e** was obtained in 99% yield as a yellowish oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.38 (m, 2H), 3.74 (s, 6H), 3.73 (s, 6H), 2.87 (m, 4H), 2.79 (d, J = 2.7 Hz, 2H), 2.71 (c, J = 2.4 Hz, 2H), 2.04 (t, J = 2.7 Hz, 1H), 1.78 (t, J = 2.4 Hz, 3H). ^{13}C NMR (75 MHz,

[262] Brummond, K. M.; Chen, H.; Fisher, K. D.; Kereker, A. D.; Rickards, B.; Sill, P. C.; Geib, S. J. *Org. Lett.* **2002**, *4*, 1931-1934.
[272] Zhang, Q.; Xu, W.; Lu, X. *J. Org. Chem.* **2005**, *70*, 1505-1507.
[277] Goeta, A.; Salter, M. M.; Shah. H. *Tetrahedron* **2006**, *62*, 3582-3599.

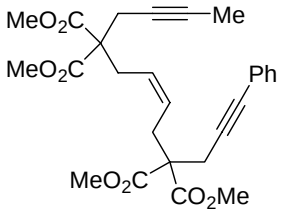
$CDCl_3$, DEPT-135) δ 170.7 (C), 170.4 (C), 127.7 (CH), 127.1 (CH), 79.5 (C), 78.9 (C), 73.5 (C), 71.8 (CH), 57.1 (C), 57.0 (C), 53.0 (CH_3), 52.9 (CH_3), 30.2 (CH_2), 30.1 (CH_2), 23.2 (CH_2), 22.9 (CH_2), 3.7 (CH_3). HRMS-FAB+ $[MH]^+$ Calc. for $C_{21}H_{27}O_8$: 407.1706; found: 407.1716.

(*Z*)-Tetramethyl 1-phenyldodeca-6-en-1,11-diyne-4,4,9,9-tetracarboxylate ((*Z*)-25f)



Starting from dimethyl propargylmalonate (0.66 mmol, Fluka) and (*Z*)-dimethyl 2-(4-bromobut-2-enyl)-2-(3-phenylprop-2-ynyl)malonate[277] (R = Ph in the intermediate of *Path B*, 0.66 mmol) and following Path B for alkylations (THF, 9 mL, 0ºC to 50ºC, 22 h), **(*Z*)-25f** was obtained in 91% yield as a sticky white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35-7.27 (m, 2H), 7.23-7.17 (m, 3H), 5.36 (m, 2H), 3.69 (s, 6H), 3.63 (s, 6H), 2.93 (s, 2H), 2.86 (t, J = 5.5 Hz, 4H), 2.71 (d, J = 2.6 Hz, 2H), 1.91 (t, J = 2.6 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, DEPT-135) δ 170.4 (C), 170.3 (C), 131.9 (CH), 128.3 (CH), 128.2 (CH), 127.6 (CH), 127.4 (CH), 123.3 (C), 84.3 (C), 83.9 (C), 78.9 (C), 71.8 (CH), 57.3 (C), 57.0 (C), 53.0 (CH_3), 52.9 (CH_3), 30.3 (CH_2), 30.2 (CH_2), 23.9 (CH_2), 23.0 (CH_2). HRMS-FAB+ $[MH]^+$ Calc. for $C_{26}H_{29}O_8$: 469.1862; found: 469.1877.

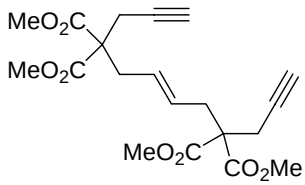
(*Z*)-Tetramethyl 1-phenyltrideca-6-en-1,11-diyne-4,4,9,9-tetracarboxylate ((*Z*)-25g)



[277] Goeta, A.; Salter, M. M.; Shah. H. *Tetrahedron* **2006**, *62*, 3582-3599.

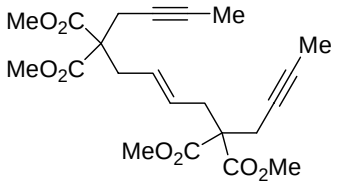
Starting from dimethyl 2-(but-2-ynyl)malonate[272] (0.52 mmol) and (*Z*)-dimethyl 2-(4-bromobut-2-enyl)-2-(3-phenylprop-2-ynyl)malonate[277] (R = Ph in the intermediate of *Path B*, 0.52 mmol) and following Path B for alkylations (THF, 9 mL, 0ºC to 50ºC, 18 h), **(*Z*)-25g** was obtained in 75% yield as a yellowish oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44-7.36 (m, 2H), 7.31-7.24 (m, 3H), 5.42 (m, 2H), 3.77 (s, 6H), 3.71 (s, 6H), 3.01 (s, 2H), 2.94 (m, 4H), 2.72 (c, J = 2.4 Hz, 2H), 1.72 (t, J = 2.4 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, DEPT-135) δ 170.7 (C), 170.5 (C), 131.9 (CH), 128.4 (CH), 128.2 (CH), 127.8 (CH), 127.3 (CH), 123.4 (C), 84.4 (C), 83.4 (C), 79.5 (C), 73.5 (CH), 57.4 (C), 57.3 (C), 53.0 (CH_3), 52.8 (CH_3), 30.4 (CH_2), 30.2 (CH_2), 23.9 (CH_2), 23.3 (CH_2), 3.6 (CH_3). HRMS-FAB+ $[MH]^+$ Calc. for $C_{27}H_{31}O_8$: 483.2019; found: 483.2029.

(*E*)-Tetramethyl dodeca-6-en-1,11-diyne-4,4,9,9-tetracarboxylate ((*E*)-25a)



Starting from dimethyl propargylmalonate (5.24 mmol, Fluka) and (*E*)-dibromo-2-butene (2.34 mmol, Aldrich) and following Path A for alkylations (THF, 20 mL, 0ºC to 50ºC, 23 h), **(*E*)-25a** was obtained in 91% yield as a crystalline white solid (mp 104-106 ºC). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.41 (m, 2H), 3.74 (s, 12H), 2.79-2.75 (m, 8H), 2.02 (t, J = 2.6 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$, DEPT-135) δ 170.3 (C), 128.8 (CH), 79.0 (C), 71.7 (CH), 57.0 (C), 53.0 (CH_3), 35.5 (CH_2), 22.8 (CH_2). HRMS-FAB+ $[MH]^+$ Calc. for $C_{20}H_{25}O_8$: 393.1549; found: 393.1557.

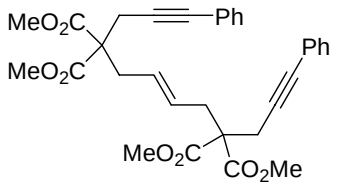
(*E*)-Tetramethyl tetradeca-7-en-2,12-diyne-5,5,10,10-tetracarboxylate ((*E*)-25b)



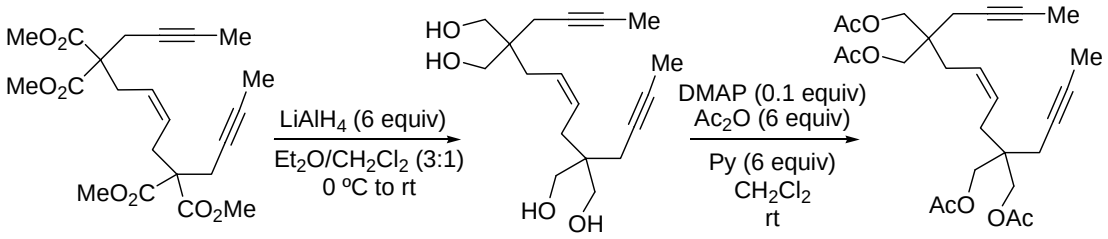
[272] Zhang, Q.; Xu, W.; Lu, X. *J. Org. Chem.* **2005**, *70*, 1505-1507.
[277] Goeta, A.; Salter, M. M.; Shah. H. *Tetrahedron* **2006**, *62*, 3582-3599.

Starting from dimethyl 2-(but-2-ynyl)malonate[272] (2.45 mmol) and (*E*)-dibromo-2-butene (1.17 mmol, Aldrich) and following Path A for alkylations (THF, 9 mL, 0ºC to 50ºC, 18 h), **(*E*)-25b** was obtained in 92% yield as a crystalline white solid (mp 91-93 ºC). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.39 (m, 2H), 3.72 (s, 12H), 2.75-2.69 (m, 8H), 1.75 (t, J = 2.5 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$, DEPT-135) δ 170.6 (C), 128.8 (CH), 79.1 (C), 73.5 (C), 57.4 (C), 52.8 (CH_3), 35.5 (CH_2), 23.1 (CH_2), 3.6 (CH_3). HRMS-FAB+ $[MH]^+$ Calc. for $C_{22}H_{29}O_8$: 421.1862; found: 421.1860.

(*E*)-Tetramethyl 1,12-diphenyldodeca-6-en-1,11-diyne-4,4,9,9-tetracarboxylate ((*E*)-25c)

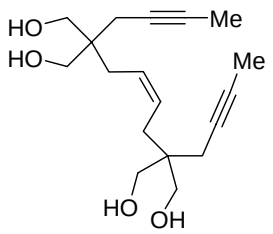


Starting from dimethyl 2-(3-phenylprop-2-ynyl)malonate[261] (3.50 mmol) and (*E*)-dibromo-2-butene (1.17 mmol, Aldrich) and following Path A for alkylations (THF, 10 mL, 0ºC to 50ºC, 40 h), **(*E*)-25c** was obtained in 84% yield as a crystalline white solid (mp 85-87 ºC). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40-7.33 (m, 4H), 7.30-7.22 (m, 6H), 5.51 (m, 2H), 3.75 (s, 12H), 3.01 (s, 4H), 2.84 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$, DEPT-135) δ 170.4 (C), 131.9 (CH), 129.0 (CH), 128.4 (CH), 128.2 (CH), 123.4 (C), 84.4 (C), 83.9 (C), 57.4 (C), 53.0 (CH_3), 35.7 (CH_2), 23.8 (CH_2). HRMS-FAB+ $[MH]^+$ Calc. for $C_{32}H_{33}O_8$: 545.2175; found: 545.2183.



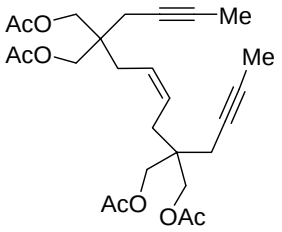
[261] Schiller, R.; Pour, M.; Fakova, H.; Kunes, J.; Cisarova, I. *J. Org. Chem.* **2004**, *69*, 6761-6765.
[272] Zhang, Q.; Xu, W.; Lu, X. *J. Org. Chem.* **2005**, *70*, 1505-1507.

(*Z*)-5,5,10,10-Tetra(hydroxymethyl)-7-en-2,12-diyne



A solution of enediyne **(*Z*)-25b** (1.9 g, 4.52 mmol) in a mixture of Et_2O/CH_2Cl_2 (50 mL) was added dropwise to a suspension of $LiAlH_4$ (1.2 g, 31.6 mmol) in Et_2O (10 mL) at 0 °C. After stirring for 24 h at room temperature, the reaction mixture was treated with aqueous 1 N NaOH. The resultant white suspension was dried over $MgSO_4$ and filtered through a short pad of Celite® topped with a thin layer of $MgSO_4$. The combined filtrate and washings were concentrated to give crude (*Z*)-2,7-di(but-2-ynyl)-2,7-bis(hydroxymethyl)oct-4-ene-1,8-diol (76%) as a white solid (mp 88-90 ºC). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.57 (t, J = 4.92 Hz, 2H), 3.59 (m, 8H), 2.91 (bs, 4H), 2.25 (d, J = 5.57 Hz, 4H), 2.11 (c, J = 2.48 Hz, 4H), 1.79 (t, J = 2.48 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$, DEPT-135) δ 127.3 (CH), 78.5 (C), 75.3 (C), 67.1 (CH_2), 42.8 (C), 28.7 (CH_2), 22.1 (CH_2), 3.7 (CH_3). HRMS-ESI+ $[MH]^+$ Calc. for $C_{18}H_{29}O_4$: 309.2060; found: 309.2054.

(*Z*)-5,5,10,10-Tetra(acetoxymethyl)-7-en-2,12-diyne ((*Z*)-25h)



To a solution of enediyne (*Z*)-2,7-di(but-2-ynyl)-2,7-bis(hydroxymethyl)oct-4-ene-1,8-diol (0.300 g, 0.974 mmol) and DMAP (10 mg, 0.09 mmol) in CH_2Cl_2 (10 mL) was added pyridine (0.5 mL, 5.84 mmol) and later acetic anhydride (0.6 mL, 5.840 mmol) under Ar, and the mixture was stirred at room temperature for 20 h at rt. Water was added slowly to quench the reaction, and the reaction mixture was extracted with EtOAc. The combined organic extracts were washed with brine, dried over MgSO4,

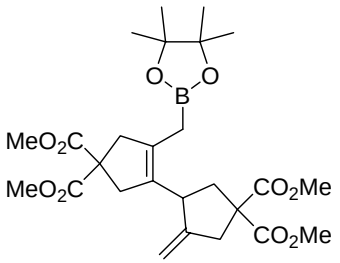
filtered and concentrated. The crude oil was purified by flash chromatography on silica gel using hexane/EtOAc (20:1) as eluent to give enediyne **(*Z*)-25h** (46%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.51 (t, J = 5.11 Hz, 2H), 3.95 (m, 8H), 2.20 (d, J = 5.84 Hz, 4H), 2.15 (c, J = 2.48 Hz, 4H), 2.03 (s, 12H), 1.75 (t, J = 2.44 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$, DEPT-135) δ 170.8 (C), 127.2 (CH), 78.8 (C), 74.0 (C), 65.6 (CH_2), 40.6 (C), 29.2 (CH_2), 22.5 (CH_2), 20.9 (CH_3), 3.6 (CH_3). HRMS-ESI+ $[MH]^+$ Calc. for $C_{26}H_{37}O_8$: 477.2482; found: 477.2491.

3.2 General optimized procedure for the synthesis of allylboronates from 6-ene-1,11-diynes

The corresponding endiyne (*ca.* 100 mg), bis(pinacolato)diboron (1.2 equiv), and $Pd(OAc)_2$ (5 mol%) were sequentially added to a 5 mL flask. After purging with Ar, dry toluene (2 mL) and MeOH (1 equiv) were added. The mixture was heated at 50ºC for the indicated time. After cooling to room temperature, Celite® was added and solvent was evaporated. Column chromatography (hexane/EtOAc) afforded the product. To obtain the highest possible yield, a 2.3 cm diameter column filled with 12-16 cm height of silicagel was used. Partial decomposition of the boronate was detected when using longer columns or retention times, probably due to hydrolysis.

3.2.1 Experimental data of allylboronates

Tetramethyl 5'-methylene-5-[(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl]-1,1'-bi(cyclopentan)-5-ene-3,3,3',3'-tetracarboxylate (26a)



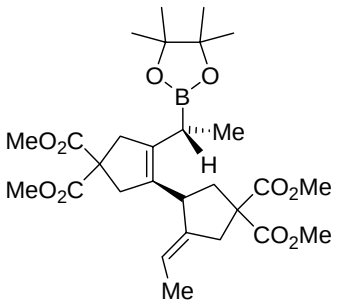
Following general borylative polycyclization procedure, **26a** was obtained as a colorless oil, and depending upon the starting enediyne:

- From **(*Z*)-25a**: 5.5 h. Hexane/EtOAc 5:1, 38% (isolated).

- From **(*E*)-25a**: 18 h. Hexane/EtOAc 4:1, 36% (calculated by NMR).

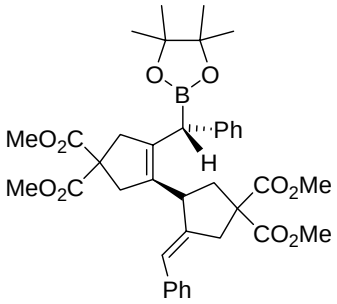
^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.89 (m, 1H), 4.68 (m, 1H), 3.73 (s, 3H), 3.71 (s, 3H), 3.70 (s, 3H), 3.68 (s, 3H), 3.48 (m, 1H), 3.12-2.78 (m, 6H), 2.45 (ddd, J = 13.1, 7.8, 1.3 Hz, 1H), 2.03 (m, 1H), 1.66 (m, 2H), 1.20 (s, 12H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.9 (C), 172.8 (C), 172.3 (C), 172.2 (C), 148.6 (C), 132.6 (C), 130.2 (C), 107.8 (CH_2), 83.5 (C), 58.8 (C), 57.6 (C), 53.0 (CH_3), 52.9 (CH_3), 52.8 (CH_3), 52.7 (CH_3), 45.4 (CH_2), 41.9 (CH), 40.5 (CH_2), 39.5 (CH_2), 38.1 (CH_2), 24.9 (CH_3), 12.5 (CH_2, HMQC). HRMS-FAB+ $[M]^+$ Calc. for $C_{26}H_{37}BO_{10}$: 520.2480; found: 520.2493.

(*rac*)-Tetramethyl (1'*S*,5'*E*)-5'-ethylidene-5-[(1*R*)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl]-1,1'-bi(cyclopentan)-5-ene-3,3,3',3'-tetracarboxylate (26b)



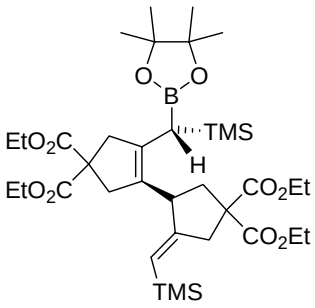
Following general borylative polycyclization procedure, **26b** was obtained after 7.5 h in 83% yield as a colorless oil (hexane/EtOAc 6:1), mp 103-106 ºC. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.99 (m, 1H), 3.74 (s, 3H), 3.73 (s, 3H), 3.70 (s, 3H), 3.69 (s, 3H), 3.48 (m, 1H), 3.19-2.99 (m, 2H), 2.94-2.70 (m, 4H), 2.43 (ddd, J = 12.7, 7.3, 1.5 Hz, 1H), 2.14 (c, J = 7.4 Hz, 1H), 2.01 (t, J = 12.7 Hz, 1H), 1.57 (m, 3H), 1.20 (s, 12H), 1.06 (d, J = 7.6 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.9 (C), 172.8 (C), 172.5 (C), 172.4 (C), 139.5 (C), 138.4 (C), 130.6 (C), 117.3 (CH), 83.3 (C), 58.9 (C), 57.8 (C), 52.9 (CH_3), 52.8 (CH_3), 52.7 (CH_3), 42.2 (CH_2), 41.8 (CH), 39.4 (CH_2), 38.4 (CH_2), 37.2 (CH_2), 24.9 (CH_3), 24.8 (CH_3), 17.8 (CH, HMQC), 14.8 (CH_3), 14.7 (CH_3). HRMS-FAB+ $[MH]^+$ Calc. for $C_{28}H_{42}BO_{10}$: 549.2871; found: 549.2876.

(*rac*)- Tetramethyl (1'*S*,5'*E*)-5'-benzylidene-5-[(*R*)-phenyl(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl]-1,1'-bi(cyclopentan)-5-ene-3,3,3',3'-tetracarboxylate (26c)



Following general borylative polycyclization procedure, **26c** was obtained after 7 h in 65% yield as a sticky colorless oil (hexane/EtOAc 6:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.40-7.12 (m, 10H), 5.97 (m, 1H), 3.91 (m, 1H), 3.76 (s, 3H), 3.75 (s, 3H), 3.71 (s, 3H), 3.65 (s, 1H), 3.55 (s, 3H), 3.45 (m, 1H), 3.23-2.82 (m, 5H), 2.54 (ddd, J = 12.8, 7.2, 1.3 Hz, 1H), 2.11 (t, J = 12.6 Hz, 1H), 1.26 (s, 6H), 1.25 (s, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.6 (C), 172.5 (C), 172.1 (C), 172.0 (C), 141.4 (C), 140.3 (C), 137.9 (C), 136.9 (C), 132.2 (C), 129.4 (CH), 128.5 (CH), 128.4 (CH), 128.3 (CH), 126.4 (CH), 125.9 (CH), 123.7 (CH), 83.8 (C), 59.7 (C), 57.6 (C), 53.1 (CH_3), 53.0 (CH_3), 52.8 (CH_3), 52.7 (CH_3), 43.7 (CH), 43.1 (CH_2), 39.5 (CH_2), 39.1 (CH_2), 37.5 (CH_2), 32.3 (CH, HMQC), 24.9 (CH_3), 24.8 (CH_3). HRMS-ESI+ $[M+NH_4]^+$ Calc. for $C_{38}H_{49}BNO_{10}$: 690.3444; found: 690.3429.

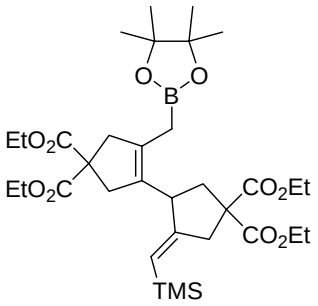
(*rac*)- Tetraethyl (1'*R*,5'*E*)-5-[(*S*)-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)(trimethylsilyl)methyl]-5'-[(trimethylsilyl)methylene]-1,1'-bi(cyclopentan)-5-ene-3,3,3',3'-tetracarboxylate (26d)



Following general borylative polycyclization procedure, **26d** was obtained after 24 h in 74% yield as a colorless oil (hexane/EtOAc 8:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.13 (m, 1H), 4.26-4.06 (m, 8H), 3.47 (m, 1H), 3.09 (m, 3H), 2.92-2.67 (m, 3H), 2.37 (ddd, J = 13.1, 7.9, 1.5 Hz, 1H), 1.99 (t, J = 12.6 Hz, 1H), 1.72 (s, 1H), 1.28-1.20 (m, 12H),

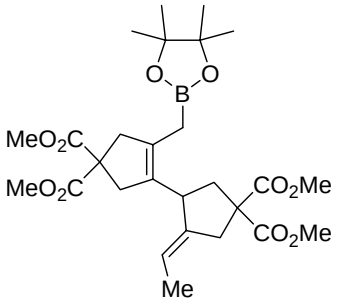
1.19 (s, 6H), 1.17 (s, 6H), 0.07 (s, 9H), 0.06 (s, 9H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.6 (C), 172.5 (C), 171.9 (C), 171.8 (C), 157.7 (C), 135.0 (C), 128.2 (C), 121.4 (CH), 82.9 (C), 61.6 (CH_2), 61.5 (CH_2), 61.3 (CH_2), 59.2 (C), 57.7 (C), 45.1 (CH_2), 44.7 (CH), 40.4 (CH_2), 38.7 (CH_2), 37.4 (CH_2), 25.2 (CH_3), 24.9 (CH_3), 18.6 (CH, HMQC), 14.3 (CH_3), 14.2 (CH_3), -0.2 (CH_3), -0.3 (CH_3). HRMS-ESI+ $[MH]^+$ Calc. for $C_{36}H_{62}BO_{10}Si_2$: 721.3969; found: 721.3972.

Tetraethyl (5'*E*)-5-[(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl]-5'-[(trimethylsilyl)methylene]-1,1'-bi(cyclopentan)-5-ene-3,3,3',3'-tetracarboxylate (26d')



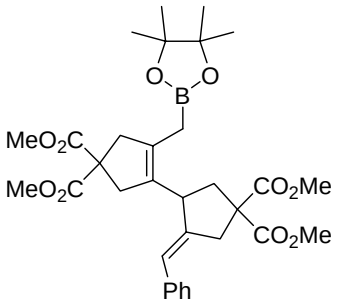
Following general borylative polycyclization procedure, **26d'** was obtained after 24 h in 5% yield as a colorless oil (hexane/EtOAc 8:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.16 (m, 1H), 4.19 (m, 8H), 3.50 (m, 1H), 3.19-2.68 (m, 6H), 2.45 (ddd, J = 13.0, 7.8, 1.6 Hz, 1H), 1.99 (m, 1H), 1.67 (m, 2H), 1.29-1.18 (m, 24H), 0.08 (s, 9H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.6 (C), 172.3 (C), 171.9 (C), 171.8 (C), 157.5 (C), 132.9 (C), 130.8 (C), 121.1 (CH), 83.5 (C), 61.7 (CH_2), 61.6 (CH_2), 61.5 (CH_2), 61.4 (CH_2), 59.4 (C), 57.7 (C), 45.5 (CH_2), 44.8 (CH), 40.4 (CH_2), 39.4 (CH_2), 37.4 (CH_2), 25.0 (CH_3), 14.3 (CH_3), 12.6 (CH_2, HMQC), -0.2 (CH_3).

Tetramethyl (5'*E*)-5'-ethylidene-5-[(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl]-1,1'-bi(cyclopentan)-5-ene-3,3,3',3'-tetracarboxylate (26e)



Following general borylative polycyclization procedure, **26e** was obtained after 4 h in 59% yield (65% calculated by NMR) as a colorless oil (hexane/EtOAc 6:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.04 (m, 1H), 3.73 (s, 3H), 3.72 (s, 3H), 3.70 (s, 3H), 3.69 (s, 3H), 3.42 (m, 1H), 3.14-2.71 (m, 6H), 2.42 (ddd, J = 12.7, 7.3, 1.6 Hz, 1H), 1.99 (t, J = 12.6 Hz, 1H), 1.65 (m, 2H), 1.56 (m, 3H), 1.21 (s, 12H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.9 (C), 172.8 (C), 172.5 (C), 172.4 (C), 139.2 (C), 132.5 (C), 130.7 (C), 117.2 (CH), 83.4 (C), 58.9 (C), 57.7 (C), 53.0 (CH_3), 52.9 (CH_3), 52.8 (CH_3), 52.7 (CH_3), 45.5 (CH_2), 41.9 (CH), 39.6 (CH_2), 38.3 (CH_2), 37.1 (CH_2), 24.9 (CH_3), 24.9 (CH_3), 14.7 (CH_3), 12.0 (CH_2, HMQC). HRMS-FAB+ $[M]^+$ Calc. for $C_{27}H_{39}BO_{10}$: 534.2636; found: 534.2651.

Tetramethyl (5'*E*)-5'-benzylidene-5-[(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl]-1,1'-bi(cyclopentan)-5-ene-3,3,3',3'-tetracarboxylate (26f)



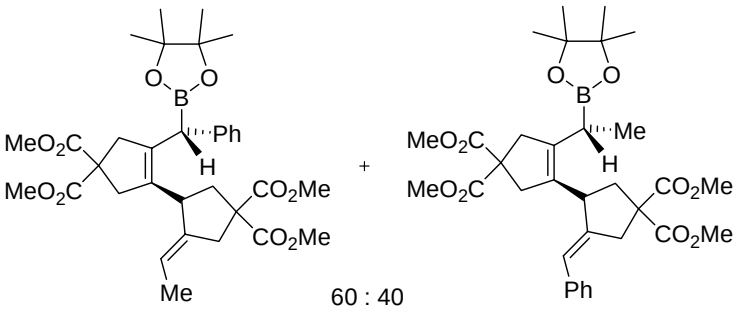
Following general borylative polycyclization procedure, **26f** was obtained after 6 h in 53% yield (63% calculated by NMR) as a colorless oil (hexane/EtOAc 5:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.36-7.13 (m, 5H), 6.08 (m, 1H), 3.74 (s, 6H), 3.72 (s, 3H), 3.65 (s, 3H), 3.43 (m, 1H), 3.21-2.83 (m, 5H), 2.50 (ddd, J = 12.8, 7.4, 1.5 Hz, 1H), 2.04 (t, J = 12.6 Hz, 1H), 1.74 (m, 2H), 1.22 (s, 12H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.8 (C), 172.7 (C), 172.2 (C), 141.6 (C), 138.2 (C), 133.5 (C), 130.4 (C), 128.5 (CH),

128.3 (CH), 126.3 (CH), 123.3 (CH), 83.5 (C), 59.6 (C), 57.7 (C), 53.0 (CH_3), 52.9 (CH_3), 52.8 (CH_3), 52.8 (CH_3), 45.5 (CH_2), 43.8 (CH), 39.7 (CH_2), 39.0 (CH_2), 37.4 (CH_2), 24.9 (CH_3), 24.9 (CH_3), 12.0 (CH_2, HMQC). HRMS-ESI+ $[M+Na]^+$ Calc. for $C_{32}H_{41}BO_{10}Na$: 619.2684; found: 619.2684.

Mixture of regioisomers (26g)

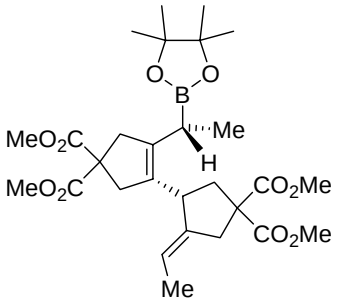
(*rac*)- Tetramethyl (1'*S*,5'*E*)-5'-ethylidene-5-[(*R*)-phenyl(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl]-1,1'-bi(cyclopentan)-5-ene-3,3,3',3'-tetracarboxylate (major)

(*rac*)- Tetramethyl (1'*S*,5'*E*)-5'-benzylidene-5-[(1*R*)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl]-1,1'-bi(cyclopentan)-5-ene-3,3,3',3'-tetracarboxylate (minor)



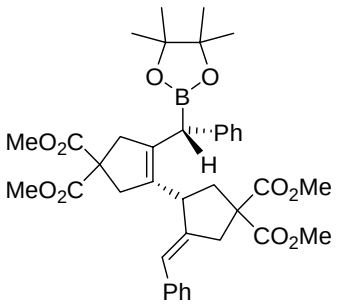
Following general borylative polycyclization procedure, mixture of two possible rioisomers **26g** (60:40) was obtained after 22 h in 72% yield as a colorless oil (hexane/EtOAc 6:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.40-7.10 (m, 10H), 6.00 (m, 1H: minor), 4.99 (m, 1H: major), 3.76 (s, 6H: minor), 3.75 (s, 6H: major), 3.72 (s, 3H: minor), 3.70 (s, 3H: major), 3.63 (s, 3H: minor), 3.61 (s, 3H: major), 3.58 (m, 1H: major), 3.44 (m, 1H: minor), 3.26-2.70 (m, 11-13H), 2.57-2.40 (m, 2H), 2.22 (c, J = 7.5 Hz, 1H: minor), 2.06 (m, 2H), 1.59 (m, 3H: major), 1.24 (s, 6H: major), 1.23 (s, 6H: major), 1.22 (s, 12H: minor), 1.14 (d, J = 7.5 Hz, 3H: minor). HRMS-ESI+ $[M+NH_4]^+$ Calc. for $C_{33}H_{47}BNO_{10}$: 628.3287; found: 628.3270.

(*rac*)- Tetramethyl (1'*R*,5'*E*)-5'-ethylidene-5-[(1*R*)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl]-1,1'-bi(cyclopentan)-5-ene-3,3,3',3'-tetracarboxylate (26b')



Following general borylative polycyclization procedure, **26b'** was obtained after 6 h at 70 ºC in 70% yield (calculated by NMR) as a colorless oil (hexane/EtOAc 6:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.09 (m, 1H), 3.73 (s, 3H), 3.72 (s, 3H), 3.70 (s, 3H), 3.68 (s, 3H), 3.46 (m, 1H), 3.10-2.96 (m, 3H), 2.90-2.74 (m, 3H), 2.39 (ddd, J = 12.6, 7.3, 1.4 Hz, 1H), 2.15 (c, J = 7.5 Hz, 1H), 1.98 (t, J = 12.6 Hz, 1H), 1.55 (m, 3H), 1.20 (s, 6H), 1.19 (s, 6H), 1.03 (d, J = 7.6 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 173.0 (C), 172.7 (C), 172.5 (C), 172.4 (C), 139.1 (C), 138.2 (C), 130.3 (C), 117.3 (CH), 83.3 (C), 58.9 (C), 57.7 (C), 53.0 (CH_3), 52.9 (CH_3), 52.8 (CH_3), 52.6 (CH_3), 42.3 (CH_2), 41.8 (CH), 39.7 (CH_2), 38.5 (CH_2), 37.0 (CH_2), 24.9 (CH_3), 24.8 (CH_3), 18.0 (CH, HMQC), 14.7 (CH_3), 14.5 (CH_3). HRMS-FAB+ $[M]^+$ Calc. for $C_{28}H_{41}BO_{10}$: 548.2793; found: 548.2772.

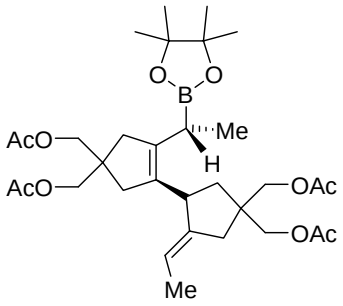
(*rac*)- Tetramethyl (1'*R*,5'*E*)-5'-benzylidene-5-[(*R*)-phenyl(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl]-1,1'-bi(cyclopentan)-5-ene-3,3,3',3'-tetracarboxylate (26c')



Following general borylative polycyclization procedure, **26c'** was obtained after 21.5 h in 46% yield (calculated by NMR) as a sticky colorless oil (hexane/EtOAc 5:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.40-7.10 (m, 10H), 6.16 (m, 1H), 3.95 (m, 1H), 3.77 (s, 3H), 3.76 (s, 3H), 3.69 (m, 1H), 3.66 (s, 3H), 3.64 (s, 3H), 3.53-3.17 (m, 3H), 2.95 (bs, 2H), 2.87 (m,1H), 2.53 (m, 1H), 2.09 (m, 1H), 1.28 (s, 12H). ^{13}C-NMR (75 MHz,

$CDCl_3$, DEPT-135) δ 172.7 (C), 172.5 (C), 172.2 (C), 172.1 (C), 141.6 (C), 140.2 (C), 138.2 (C), 137.0 (C), 132.2 (C), 129.4 (CH), 128.6 (CH), 128.5 (CH), 128.4 (CH), 125.9 (CH), 123.6 (CH), 83.9 (C), 59.7 (C), 57.7 (C), 53.1 (CH_3), 53.0 (CH_3), 52.8 (CH_3), 43.9 (CH), 42.8 (CH_2), 39.6 (CH_2), 39.1 (CH_2), 37.6 (CH_2), 32.1 (CH, HMQC), 25.1 (CH_3), 25.0 (CH_3). HRMS-ESI+ $[M+NH_4]^+$ Calc. for $C_{38}H_{49}BNO_{10}$: 690.3444; found: 690.3450.

(*rac*)- [(1'*S*,5'*E*)-5'-Ethylidene-5-[(1*R*)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl]-1,1'-bi(cyclopentan)-5-ene-3,3,3',3'-tetrayl]tetra(methylene) tetraacetate (26h)



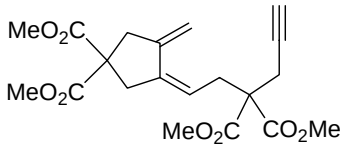
Following general borylative polycyclization procedure, **26h** was obtained after 15 h in 80% yield as a colorless oil (hexane/EtOAc 2.5:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.00 (m, 1H), 3.98 (m, 8H), 3.52 (m, 1H), 2.37-1.94 (m, 7H), 2.04 (s, 6H), 2.03 (s, 3H), 2.02 (s, 3H), 1.79-1.70 (m, 1H), 1.53 (d, J = 6.9 Hz, 3H), 1.34 (t, J = 12.2 Hz, 1H), 1.17 (s, 12H), 1.02 (d, J = 7.4 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 171.1 (C), 171.0 (C), 140.9 (C), 137.8 (C), 131.5 (C), 117.3 (CH), 83.0 (C), 68.2 (CH_2), 67.3 (CH_2), 66.3 (CH), 65.8 (CH), 65.5 (CH_2), 44.1 (C), 42.6 (C), 41.6 (C), 40.8 (CH), 40.4 (CH_2), 37.5 (CH_2), 36.1 (CH_2), 35.5 (CH_2), 24.7 (CH_3), 24.6 (CH_3), 20.8 (CH_3), 17.8 (CH, HMQC), 14.6 (CH_3), 14.5 (CH_3). HRMS-ESI+ $[M+NH_4]^+$ Calc. for $C_{32}H_{53}BNO_{10}$: 622.3757; found: 622.3727.

3.3 General optimized procedure for the synthesis of 1,3-dienes and tricycles from 6-ene-1,11-diynes

The corresponding endiyne (*ca.* 100 mg) and $Pd(OAc)_2$ (0.05 equiv) were added to a 5 mL flask. After purging with Ar, dry toluene (2 mL) and MeOH (1 equiv) were added. The mixture was heated at 50ºC for the indicated time. After cooling to room temperature, Celite® was added and solvent was evaporated. Column chromatography (hexane/EtOAc) afforded the product.

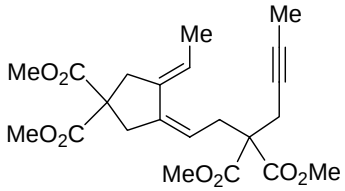
3.3.1 Experimental data of 1,3-dienes

(*Z*)-Dimethyl 3-(3,3-bis(methoxycarbonyl)hex-5-ynylidene)-4-methylenecyclopentane-1,1-dicarboxylate ((*Z*)-27a)



Following general cyclization procedure, **(*Z*)-27a** was obtained after 7.5 h in 21% yield as a colorless oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.36 (s, 1H), 5.28 (t, J = 7.0 Hz, 1H), 5.18 (s, 1H), 3.73 (s, 6H), 3.71 (s, 6H), 3.04 (m, 4H), 2.97 (bs, 2H), 2.81 (d, J = 2.6 Hz, 2H), 1.97 (t, J = 2.6 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 171.7 (C), 170.4 (C), 143.5 (C), 138.8 (C), 119.7 (CH), 112.1 (CH_2), 78.9 (C), 71.7 (C), 57.5 (C), 57.2 (C), 53.0 (CH_3), 52.9 (CH_3), 43.0 (CH_2), 42.9 (CH_2), 31.8 (CH_2), 23.3 (CH_2). HRMS-FAB+ $[MH]^+$ Calc. for $C_{20}H_{25}O_8$: 393.1549; found: 393.1560.

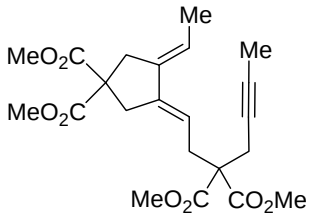
(3*Z*,4*E*)-Dimethyl 3-(3,3-bis(methoxycarbonyl)hept-5-ynylidene)-4-ethylidenecyclopentane-1,1-dicarboxylate ((*Z*)-27b)



Following general cyclization procedure, **(*Z*)-27b** was obtained after 19 h in less than 15% yield as a colorless oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.91 (m, 1H), 5.12 (t, J = 6.9 Hz, 1H), 3.71 (s, 6H), 3.70 (s, 6H), 2.98 (m, 4H), 2.91 (m, 2H), 2.72 (c, J = 2.5 Hz,

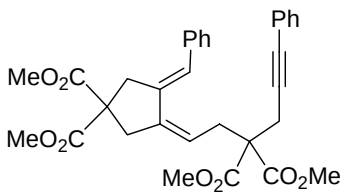
2H), 1.77-1.68 (m, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.0 (C), 170.8 (C), 139.6 (C), 136.4 (C), 122.9 (CH), 117.0 (CH), 79.0 (C), 73.5 (C), 57.5 (C), 57.3 (C), 52.9 (CH_3), 52.8 (CH_3), 43.5 (CH_2), 38.5 (CH_2), 31.5 (CH_2), 23.4 (CH_2), 15.5 (CH_3), 3.6 (CH_3).

(3E,4E)-dimethyl 3-(3,3-bis(methoxycarbonyl)hept-5-ynylidene)-4-ethylidenecyclopentane-1,1-dicarboxylate ((*E*)-27b)



Following general cyclization procedure, **(*E*)-27b** was obtained after 24 h at 70 ºC in less than 15% yield as a colorless oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.81 (m, 1H), 5.45 (m, 1H), 3.73 (s, 6H), 3.72 (s, 6H), 3.06 (bs, 2H), 2.94 (bs, 2H), 2.85 (d, J = 7.9 Hz, 2H), 2.73 (c, J = 2.5 Hz, 2H), 1.76 (t, J = 2.5 Hz, 3H), 1.69 (d, J = 7.0 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.1 (C), 170.8 (C), 141.2 (C), 137.3 (C), 115.7 (CH), 111.8 (CH), 79.2 (C), 73.8 (C), 57.6 (C), 57.5 (C), 53.0 (CH_3), 52.9 (CH_3), 38.2 (CH_2), 37.7 (CH_2), 32.5 (CH_2), 23.3 (CH_2), 14.9 (CH_3), 3.7 (CH_3). HRMS-FAB+ $[MH]^+$ Calc. for $C_{22}H_{29}O_8$: 421.1862; found: 421.1875.

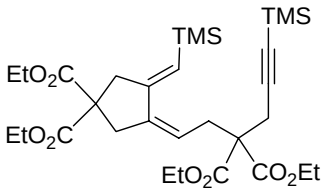
(3*E*,4*Z*)-dimethyl 3-benzylidene-4-(3,3-bis(methoxycarbonyl)-6-phenylhex-5-ynylidene)cyclopentane-1,1-dicarboxylate ((*Z*)-27c)



Following general cyclization procedure, **(*Z*)-27c** was obtained after 27 h at 70 ºC in 35% yield as a colorless oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.42-7.03 (m, 10H), 6.83 (bs, 1H), 5.32 (t, J = 7.2 Hz, 1H), 3.77 (s, 6H), 3.70 (s, 6H), 3.32 (d, J = 2.3 Hz, 2H),

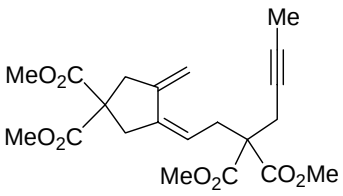
3.26 (d, J = 7.2 Hz, 2H), 3.04 (s, 2H), 2.99 (m, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 171.9 (C), 170.6 (C), 141.6 (C), 137.5 (C), 137.0 (C), 131.8 (CH), 129.3 (CH), 128.4 (CH), 128.3 (CH), 128.0 (CH), 127.6 (CH), 127.1 (CH), 123.3 (C), 118.7 (CH), 84.3 (C), 83.8 (C), 57.8 (C), 53.1 (CH_3), 42.3 (CH_2), 40.0 (CH_2), 32.0 (CH_2), 24.1 (CH_2). HRMS-FAB+ $[MH]^+$ Calc. for $C_{32}H_{33}O_8$: 545.2175; found: 545.2173.

(3*Z*,4*E*)-diethyl 3-(3,3-bis(ethoxycarbonyl)-6-(trimethylsilyl)hex-5-ynylidene)-4-((trimethylsilyl)methylene)cyclopentane-1,1-dicarboxylate ((*Z*)-27d)



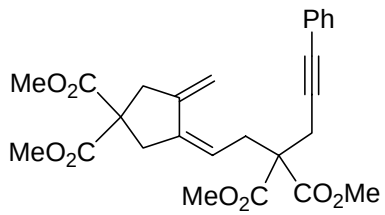
Following general cyclization procedure, **(*Z*)-27d** was obtained after 25 h at 70 ºC in less than 15% yield as a colorless oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.88 (bs, 1H), 5.29 (m, 1H), 4.19 (m, 8H), 3.12-3.01 (m, 4H), 2.94 (m, 2H), 2.82 (s, 2H), 1.24 (m, 12H), 0.16 (s, 9H), 0.11 (s, 9H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 171.4 (C), 170.0 (C), 151.7 (C), 140.1 (C), 127.4 (CH), 120.1 (CH), 61.7 (CH_2), 57.7 (C), 57.4 (C), 42.2 (CH_2), 31.7 (CH_2), 24.5 (CH_2), 14.2 (CH_3), 0.2 (CH_3), -0.1 (CH_3). HRMS-FAB+ $[MH]^+$ Calc. for $C_{30}H_{49}O_8Si_2$: 593.2966; found: 593.2969.

(*Z*)-dimethyl 3-(3,3-bis(methoxycarbonyl)hept-5-ynylidene)-4-methylenecyclopentane-1,1-dicarboxylate ((*Z*)-27e)



Following general cyclization procedure, **(*Z*)-27e** was obtained after 22 h in less than 15% yield as a colorless oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.37 (s, 1H), 5.29 (t, J = 7.0 Hz, 1H), 5.19 (s, 1H), 3.71 (s, 12H), 3.05-2.95 (m, 6H), 2.75 (c, J = 2.5 Hz, 2H), 1.72 (t, J = 2.5 Hz, 3H).

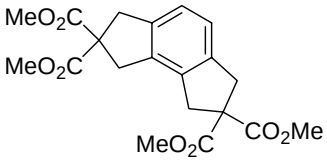
(*Z*)-dimethyl 3-(3,3-bis(methoxycarbonyl)-6-phenylhex-5-ynylidene)-4-methylenecyclopentane-1,1-dicarboxylate ((*Z*)-27f)



Following general cyclization procedure, **(*Z*)-27f** was obtained after 24 h at 70 ºC in 15% yield as a colorless oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.38-7.19 (m, 5H), 5.38 (s, 1H), 5.33 (t, J = 7.2 Hz, 1H), 5.16 (s, 1H), 3.73 (s, 6H), 3.69 (s, 6H), 3.10 (d, J = 7.2 Hz, 2H), 3.05-2.96 (m, 6H). HRMS-FAB+ $[M]^+$ Calc. for $C_{26}H_{28}O_8$: 468.1784; found: 468.1771.

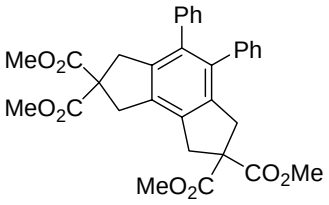
3.3.2 Experimental data of tricycles

Tetramethyl 1,3,6,8-tetrahydro-*as*-indacene-2,2,7,7-tetracarboxylate (28a)



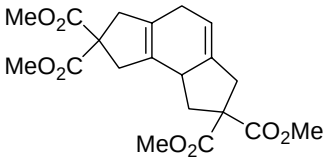
This product were obtained heating **29a** at atmospheric conditions. Crystalline white solid (mp 129-132 ºC). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.00 (s, 2H), 3.75 (s, 12H), 3.56 (s, 4H), 3.51 (s, 4H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.3 (C), 139.0 (C), 135.8 (C), 123.0 (CH), 60.5 (C), 53.2 (CH_3), 40.6 (CH_2), 39.2 (CH_2). HRMS-GC/EI+ $[M]^+$ Calc. for $C_{20}H_{22}O_8$: 390.1315; found: 390.1328.

Tetramethyl 4,5-diphenyl-1,3,6,8-tetrahydro-*as*-indacene-2,2,7,7-tetracarboxylate (28b)



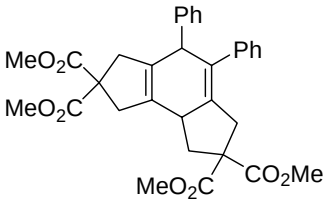
This product were obtained heating **29b** at atmospheric conditions. Crystalline white solid (mp 184-186 ºC). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.20-7.06 (m, 6H), 7.04-6.96 (m, 4H), 3.73 (s, 12H), 3.63 (s, 4H), 3.41 (s, 4H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.3 (C), 139.5 (C), 138.6 (C), 136.6 (C), 134.6 (C), 130.1 (CH), 127.9 (CH), 126.5 (CH), 60.2 (C), 53.2 (CH_3), 40.9 (CH_2), 39.5 (CH_2). HRMS-FAB+ $[M]^+$ Calc. for $C_{32}H_{30}O_8$: 542.1941; found: 542.1946.

Tetramethyl 1,3,4,6,8,8a-hexahydro-*as*-indacene-2,2,7,7-tetracarboxylate (29a)



Following general cyclization procedure, **29a** was obtained after 5 h in 30% yield as a crystalline white solid (mp 92-95 ºC). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.50 (m, 1H), 3.75 (s, 3H), 3.74 (s, 3H), 3.73 (s, 3H), 3.71 (s, 3H), 3.12-2.82 (m, 7H), 2.73-2.57 (m, 3H), 1.97 (t, J = 12.3 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 173.0 (C), 172.9 (C), 172.8 (C), 172.4 (C), 139.1 (C), 131.5 (C), 130.7 (C), 116.0 (CH), 58.2 (C), 57.5 (C), 53.0 (CH_3), 53.0 (CH_3), 52.9 (CH_3), 43.3 (CH_2), 42.0 (CH_2), 39.8 (CH), 38.8 (CH_2), 38.3 (CH_2), 28.0 (CH_2). HRMS-FAB+ $[MH]^+$ Calc. for $C_{20}H_{25}O_8$: 393.1549; found: 393.1555.

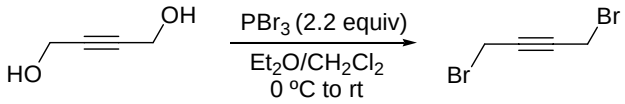
Tetramethyl 4,5-diphenyl-1,3,4,6,8,8a-hexahydro-*as*-indacene-2,2,7,7-tetracarboxylate (29b)



Following general cyclization procedure, **29b** was obtained after 22.5 h at 70 ºC in 70% yield as a crystalline white solid (mp 127-129 ºC). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.12-6.98 (m, 6H), 6.86 (m, 2H), 6.73 (m, 2H), 4.09 (m, 1H), 3.73 (s, 3H), 3.72 (s, 3H), 3.71 (s, 3H), 3.63 (s, 3H), 3.27-2.80 (m, 6H), 2.69 (m, 1H), 2.50 (m, 1H), 1.98 (t, J = 12.6 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.9 (C), 172.7 (C), 172.6 (C), 172.5 (C), 141.3 (C), 140.5 (C), 135.0 (C), 134.3 (C), 132.0 (C), 131.1 (C), 128.9 (CH), 128.2 (CH), 127.9 (CH), 126.5 (CH), 126.4 (CH), 58.1 (C), 57.6 (C), 53.0 (CH_3), 52.9 (CH_3), 52.8 (CH_3), 49.7 (CH_3), 42.2 (CH_2), 42.0 (CH_2), 40.8 (CH), 39.1 (CH_2), 36.9 (CH_2). HRMS-FAB+ $[MH]^+$ Calc. for $C_{32}H_{33}O_8$: 545.2160; found: 545.2175.

4. Pd-Catalyzed Borylative Bicyclization of 1-Ene-6,11-diynes to Alkylboronates

Two different alkyne linkers were used, 1,4-dichloro-2-butyne, purchased from Aldrich, and 1,4-dibromo-2-butyne prepared according to the next procedure:

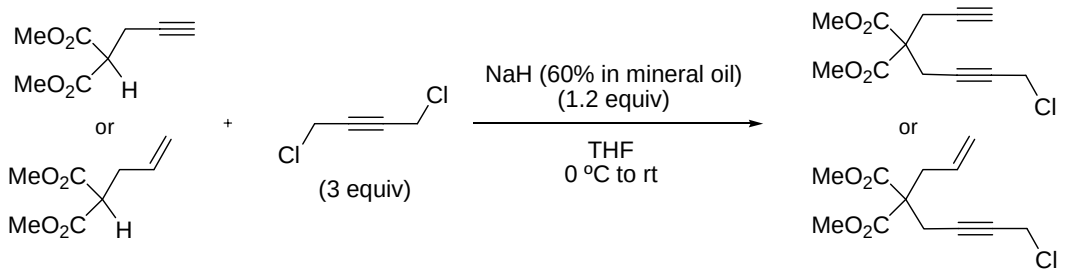


To a solution of buten-1,4-diol (1.5 g, 17.42 mmol) in a mixture of Et_2O/CH_2Cl_2 (40 mL, 1:1) at 0 ºC was added dropwise PBr_3 (3.60 mL, 38.33 mmol) for 10 min. After addition the mixture was stirred at 0 ºC for 30 min. and then was warmed to rt for 4.5 h. Next, a solution of $NaHCO_3$ (5%) was added carefully at 0 ºC until the initial orange solution turned to colorless. Extractive work-up with Et_2O, drying over $MgSO_4$, filtration, and finally evaporation of the solvent afforded the dibromide compound as a yellowish oil (2.60 g, 12.27 mmol) without further purification (70% yield).

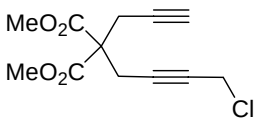
From this point, intermediate substrates and 1-ene-6, 11-diynes were prepared by the next general procedure for alkylation of malonate derivatives, bis(sulfonyl)methane

derivatives, alcohols and 4-toluenesulfonamides. Those intermediates prepared according to reported procedures will be noted.

General procedure for alkylation: To a suspension of NaH (60% in mineral oil, 1.2 equiv) in anhydrous THF or DMF (solvent and volume will be indicated in each case) under Ar atmosphere at 0 ºC, was slowly added the corresponding nucleophile (1 equiv) and the mixture was stirred at rt for 5-10 min. (formation of H_2 bubbles were observed during the addition). Then, the corresponding electrophile (1.0-3.0 equiv) was added dropwise and the mixture was allow to reaction at rt or heated (will be specified in each case). Screening by TLC indicated the completion of the reaction. Then, in the case of THF, most of the solvent was removed under vacuum and later, water and Et_2O were added into the resulting mixture. The aqueous layer was separated and extracted successively with Et_2O. In the case of DMF, similar extractive work-up with Et_2O/aq. solution of HCl (5-10%). The combined organic phases were dried over anhydrous Mg_2SO_4 and filtered through anhydrous Na_2SO_4. The solvent was removed under vacuum and the residue was purified by column chromatography (hexane/EtOAc).



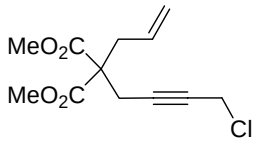
Dimethyl 2-(4-chlorobut-2-ynyl)-2-(prop-2-ynyl)malonate



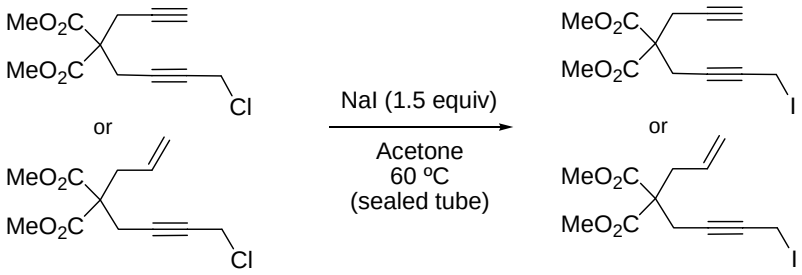
Starting from dimethyl propargylmalonate (11.75 mmol, Fluka) and 1,4-dichloro-2-butyne (35.25 mmol, Fluka) and following general procedure for alkylation (THF, 35 mL, 0ºC to rt, 15 h), was obtained in 74% yield as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.09 (t, J = 2.3 Hz, 2H), 3.77 (s, 6H), 3.04 (t, J = 2.3 Hz, 2H), 2.97 (d, J = 2.6 Hz, 2H), 2.04 (t, J = 2.6 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, DEPT-135) δ 169.2 (C),

81.4 (C), 78.6 (C), 78.4 (C), 72.0 (C), 56.7 (C), 53.3 (CH_3), 30.7 (CH_2), 23.2 (CH_2), 23.0 (CH_2). HRMS-ESI+ $[MH]^+$ Calc. for $C_{12}H_{14}ClO_4$: 257.0575; found: 257.0568.

Dimethyl 2-allyl-2-(4-chlorobut-2-ynyl)malonate

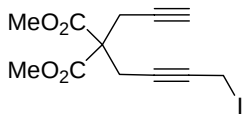


Starting from dimethyl allylmalonate (5.81 mmol, Aldrich) and 1,4-dichloro-2-butyne (17.42 mmol, Fluka) and following general procedure for alkylation (THF, 10 mL, 0ºC to rt, 24 h), was obtained in 77% yield as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.69-5.53 (m, 1H), 5.22-5.10 (m, 2H), 4.09 (t, J = 2.3 Hz, 2H), 3.74 (s, 12H), 2.84 (t, J = 2.3 Hz, 2H), 2.78 (d, J = 7.5 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, DEPT-135) δ 170.3 (C), 131.8 (CH), 120.2 (CH_2), 82.0 (C), 78.3 (C), 57.1 (C), 53.0 (CH_3), 36.9 (CH_2), 30.8 (CH_2), 23.3 (CH_2). HRMS-ESI+ $[MH]^+$ Calc. for $C_{12}H_{16}ClO_4$: 259.0731; found: 259.0733.



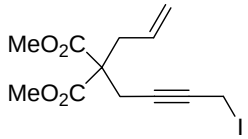
A mixture of of dimethyl 2-(4-chlorobut-2-ynyl)-2-(prop-2-ynyl)malonate or dimethyl 2-allyl-2-(4-chlorobut-2-ynyl)malonate and sodium iodide (1.5 equiv) in acetone were heated at 60 ºC in a sealed tube. After 10 h the orange mixture was cooled to rt. Then, water and Et_2O were added to the solution and two phases were separated. The organic phase was dried over $MgSO_4$ and filtered over Na_2SO_4. Evaporation of the solvent afforded the corresponding iodide compound as a yellowish oil without further purification.

Dimethyl 2-(4-iodobut-2-ynyl)-2-(prop-2-ynyl)malonate



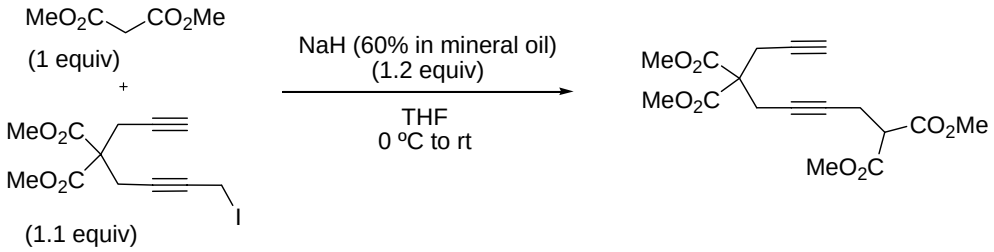
Starting from dimethyl 2-(4-chlorobut-2-ynyl)-2-(prop-2-ynyl)malonate (1.95 mmol) and NaI (2.92 mmol) in acetone (25 mL), iodide compound was obtained in 86% as a yellowish oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.78 (s, 6H), 3.64 (t, J = 2.5 Hz, 2H), 3.01 (t, J = 2.5 Hz, 2H), 2.97 (d, J = 2.6 Hz, 2H), 2.03 (t, J = 2.6 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, DEPT-135) δ 169.2 (C), 80.6 (C), 80.3 (C), 78.5 (C), 71.9 (C), 56.7 (C), 53.3 (CH_3), 23.5 (CH_2), 23.0 (CH_2), -18.5 (CH_2). HRMS-ESI+ $[MH]^+$ Calc. for $C_{12}H_{14}IO_4$: 348.9931; found: 348.9919.

Dimethyl 2-allyl-2-(4-iodobut-2-ynyl)malonate



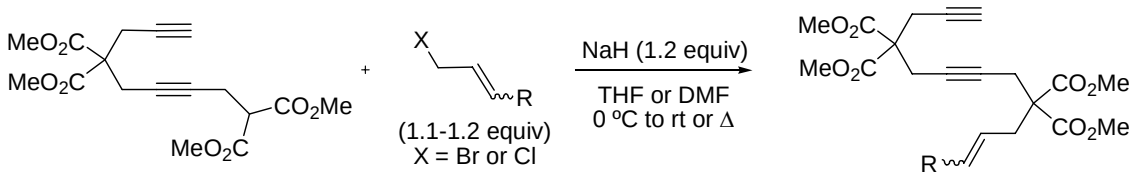
Starting from dimethyl 2-allyl-2-(4-chlorobut-2-ynyl)malonate (2.51 mmol) and NaI (3.77 mmol) in acetone (25 mL), iodide compound was obtained in 77% as a yellowish oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.68-5.54 (m, 1H), 5.19 (dc, J = 17.0, 1.6 Hz, 1H), 5.13 (d, J = 10.0 Hz, 1H), 3.74 (s, 12H), 3.65 (t, J = 2.4 Hz, 2H), 2.81 (t, J = 2.4 Hz, 2H), 2.78 (d, J = 7.5 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, DEPT-135) δ 170.3 (C), 131.9 (CH), 120.1 (CH_2), 80.9 (C), 80.3 (C), 57.2 (C), 53.0 (CH_3), 36.9 (CH_2), 23.5 (CH_2), -18.1 (CH_2). HRMS-ESI+ $[MH]^+$ Calc. for $C_{12}H_{16}IO_4$: 351.0093; found: 351.0097.

Tetramethyl nona-3,8-diyne-1,1,6,6-tetracarboxylate

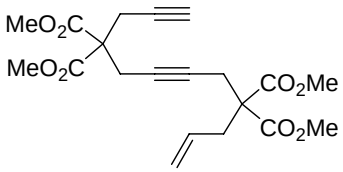


Starting from dimethyl malonate (3.16 mmol, Aldrich) and dimethyl 2-(4-iodobut-2-ynyl)-2-(prop-2-ynyl)malonate (2.87 mmol) and following general procedure for alkylation (THF, 10 mL, 0ºC to rt, 18 h), was obtained in 71% yield as a white solid (mp 43-46 ºC). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.77 (s, 6H), 3.75 (s, 6H), 3.52 (t, J = 7.7 Hz, 1H), 2.95-2.91 (m, 4H), 2.73 (dt, J = 7.7, 2.3 Hz, 2H), 2.00 (t, J = 2.6 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, DEPT-135) δ 169.3 (C), 168.5 (C), 79.5 (C), 78.7 (C), 76.7 (C), 71.7 (C), 56.8 (C), 53.2 (CH_3), 53.0 (CH_3), 51.5 (CH), 23.1 (CH_2), 22.8 (CH_2), 19.0 (CH_2). HRMS-FAB+ $[MH]^+$ Calc. for $C_{17}H_{21}O_8$: 353.1236; found: 353.1238.

4.1 Preparation and experimental data of 1-ene-6,11-diynes



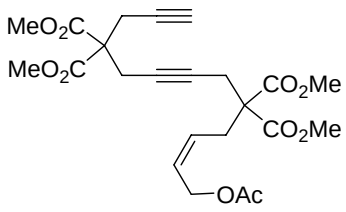
Tetramethyl dodeca-1-en-6,11-diyne-4,4,9,9-tetracarboxylate (40a)



Starting from dimethyl allylmalonate (3.92 mmol, Aldrich) and dimethyl 2-(4-iodobut-2-ynyl)-2-(prop-2-ynyl)malonate (4.31 mmol) and following general procedure for alkylation (THF, 12 mL, 0ºC to 50 ºC, 23 h), **40a** was obtained in 94% yield as a white solid (mp 65-68 ºC). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.67-5.52 (m, 1H), 5.21-5.09 (m, 2H), 3.76 (s, 6H), 3.74 (s, 6H), 2.96 (s, 2H), 2.94 (s, 2H), 2.76 (d, J = 2.4 Hz, 2H), 2.74 (d, J = 2.4 Hz, 2H), 2.01 (t, J = 2.7 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, DEPT-135) δ

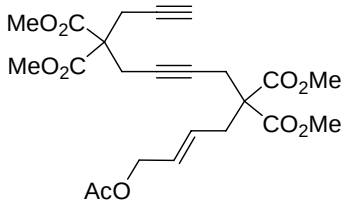
170.4 (C), 169.4 (C), 132.0 (CH), 120.0 (CH_2), 78.7 (C), 78.3 (C), 71.8 (C), 57.2 (C), 56.7 (C), 53.3 (CH_3), 52.9 (CH_3), 36.7 (CH_2), 23.1 (CH_2), 22.8 (CH_2). HRMS-ESI+ $[MH]^+$ Calc. for $C_{20}H_{25}O_8$: 393.1543; found: 393.1541.

(*Z*)-Tetramethyl 13-acetoxytrideca-11-en-1,6-diyne-4,4,9,9-tetracarboxylate (40b)



Starting from tetramethyl nona-3,8-diyne-1,1,6,6-tetracarboxylate (0.568 mmol) and (*Z*)-4-bromobut-2-enyl acetate[256] (0.681 mmol) and following general procedure for alkylation (THF, 6 mL, 0ºC to 50 ºC, 22 h), **40b** was obtained in 61% yield as a sticky oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.74-5.63 (m, 1H), 5.49-5.37 (m, 1H), 4.65 (dd, J = 6.8, 1.2 Hz, 2H), 3.75 (s, 6H), 3.74 (s, 6H), 2.95 (t, J = 2.3 Hz, 2H), 2.93 (d, J = 2.8 Hz, 2H), 2.82 (d, J = 7.9 Hz, 2H), 2.76 (t, J = 2.3 Hz, 2H), 2.05 (s, 3H), 2.01 (t, J = 2.8 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, DEPT-135) δ 170.9 (C), 170.2 (C), 169.3 (C), 128.5 (CH), 127.5 (CH), 78.7 (C), 78.2 (C), 77.8 (C), 71.8 (C), 60.3 (CH_2), 57.1 (C), 56.6 (C), 53.3 (CH_3), 53.0 (CH_3), 30.4 (CH_2), 23.3 (CH_2), 23.1 (CH_2), 22.8 (CH_2), 21.1 (CH_3). HRMS-FAB+ $[MH]^+$ Calc. for $C_{23}H_{29}O_{10}$: 465.1761; found: 465.1763.

(*E*)-Tetramethyl 13-acetoxytrideca-11-en-1,6-diyne-4,4,9,9-tetracarboxylate ((*E*)-40b))

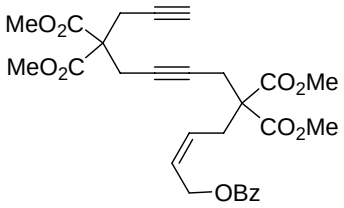


Starting from tetramethyl nona-3,8-diyne-1,1,6,6-tetracarboxylate (0.426 mmol) and (*E*)-4-bromobut-2-enyl acetate[258] (0.511 mmol) and following general procedure for alkylation (THF, 6 mL, 0ºC to 50 ºC, 20 h), **(*E*)-40b** was obtained in 30% yield as a

[256] Reppe, W. J. *Liebigs Ann. Chem.* **1935**, 80-158.

colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.77-5.66 (m, 1H), 5.60-5.49 (m, 1H), 4.49 (d, J = 6.0 Hz, 2H), 3.75 (s, 6H), 3.73 (s, 6H), 2.97-2.92 (m, 4H), 2.74 (d, J = 4.7 Hz, 2H), 2.73 (s, 2H), 2.04 (s, 3H), 2.01 (t, J = 2.6 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, DEPT-135) δ 170.8 (C), 170.2 (C), 169.3 (C), 129.4 (CH), 128.8 (CH), 78.7 (C), 78.2 (C), 77.7 (C), 71.8 (C), 64.7 (CH_2), 57.2 (C), 56.7 (C), 53.2 (CH_3), 52.9 (CH_3), 35.2 (CH_2), 23.3 (CH_2), 23.1 (CH_2), 22.8 (CH_2), 21.1 (CH_3). HRMS-ESI+ $[M+NH_4]^+$ Calc. for $C_{23}H_{32}NO_{10}$: 482.2020; found: 482.2022.

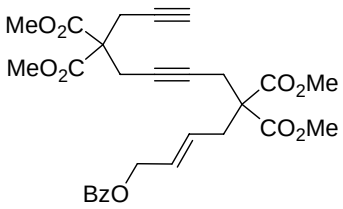
(*Z*)-Tetramethyl 13-(benzoyloxy)trideca-11-en-1,6-diyne-4,4,9,9-tetracarboxylate (40c)



Starting from tetramethyl nona-3,8-diyne-1,1,6,6-tetracarboxylate (0.568 mmol) and (*Z*)-4-bromobut-2-enyl benzoate[259] (0.681 mmol) and following general procedure for alkylation (THF, 6 mL, 0ºC to 50 ºC, 24 h), **40c** was obtained in 92% yield as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.04 (d, J = 8.4 Hz, 2H), 7.54 (t, J = 7.4 Hz, 1H), 7.42 (t, J = 7.5 Hz, 2H), 5.88-5.77 (m, 1H), 5.55-5.44 (m, 1H), 4.91 (dd, J = 6.9, 1.1 Hz, 2H), 3.74 (s, 12H), 2.95 (t, J = 2.3 Hz, 2H), 2.94 (d, J = 2.6 Hz, 2H), 2.90 (d, J = 7.9 Hz, 2H), 2.79 (t, J = 2.3 Hz, 2H), 1.99 (t, J = 2.6 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, DEPT-135) δ 170.2 (C), 169.3 (C), 166.5 (C), 133.0 (CH), 130.5 (C), 129.8 (CH), 128.6 (CH), 128.5 (CH), 127.7 (CH), 78.7 (C), 78.2 (C), 77.9 (C), 71.4 (C), 60.8 (CH_2), 57.1 (C), 56.7 (C), 53.1 (CH_3), 53.0 (CH_3), 30.5 (CH_2), 23.4 (CH_2), 23.1 (CH_2), 22.8 (CH_2). HRMS-FAB+ $[MH]^+$ Calc. for $C_{28}H_{31}O_{10}$: 527.1917; found: 527.1912.

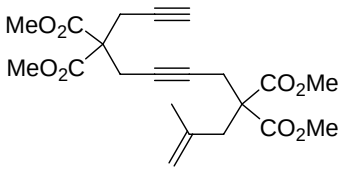
(*E*)-Tetramethyl 13-(benzoyloxy)trideca-11-en-1,6-diyne-4,4,9,9-tetracarboxylate ((*E*)-40c)

[258] Zhao, L.; Lu, X.; Xu, W. *J. Org. Chem.* **2005**, *70*, 4059-4063.
[259] Ashton, W. T.; Meurer, L. C.; Cantone, C. L.; Field, A. K. Hannah, J.; Karkas, J. D.; Liou, R.; Patel, G. F.; Perry, H. C. *J. Med. Chem.* **1988**, *31*, 2304-2315.



Starting from tetramethyl nona-3,8-diyne-1,1,6,6-tetracarboxylate (0.284 mmol) and (*E*)-4-bromobut-2-enyl benzoate[259] (0.341 mmol) and following general procedure for alkylation (THF, 6 mL, 0ºC to 50 ºC, 18 h), **((*E*)-40c** was obtained in 50% yield as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03 (d, J = 8.3 Hz, 2H), 7.54 (t, J = 7.3 Hz, 1H), 7.43 (t, J = 7.5 Hz, 2H), 5.90-5.79 (m, 1H), 5.72-5.60 (m, 1H), 4.75 (d, J = 6.0 Hz, 2H), 3.74 (s, 6H), 3.72 (s, 6H), 2.97-2.93 (m, 4H), 2.78 (d, J = 7.4 Hz, 2H), 2.76 (t, J = 2.2 Hz, 2H), 2.00 (t, J = 2.6 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, DEPT-135) δ 170.2 (C), 169.3 (C), 166.4 (C), 133.1 (CH), 130.5 (C), 129.8 (CH), 129.4 (CH), 129.1 (CH), 128.5 (CH), 78.7 (C), 78.2 (C), 77.8 (C), 71.7 (C), 65.1 (CH_2), 57.3 (C), 56.7 (C), 53.2 (CH_3), 52.9 (CH_3), 35.3 (CH_2), 23.4 (CH_2), 23.2 (CH_2), 22.3 (CH_2). HRMS-ESI+ $[M+NH_4]^+$ Calc. for $C_{28}H_{34}NO_{10}$: 544.2177; found: 544.2175.

Tetramethyl 2-methyldodeca-1-en-6,11-diyne-4,4,9,9-tetracarboxylate (40d)

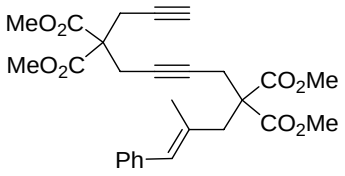


Starting from tetramethyl nona-3,8-diyne-1,1,6,6-tetracarboxylate (0.568 mmol) and 3-chloro-2-methylprop-1-ene (Aldrich) (0.681 mmol) and following general procedure for alkylation (THF, 5 mL, 0ºC to 50 ºC, 24 h), **40d** was obtained in 44% yield as a white solid (mp 48-50 ºC). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.90 (t, J = 1.5 Hz, 1H), 4.81 (s, 1H), 3.76 (s, 6H), 3.73 (s, 6H), 2.98-2.94 (m, 4H), 2.80-2.76 (m, 4H), 2.01 (t, J = 2.6 Hz, 1H), 1.63 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, DEPT-135) δ 170.8 (C), 169.3 (C), 140.1 (C), 116.4 (CH_2), 78.7 (C), 78.6 (C), 71.7 (C), 56.8 (C), 56.7 (C), 53.2 (CH_3),

[259] Ashton, W. T.; Meurer, L. C.; Cantone, C. L.; Field, A. K. Hannah, J.; Karkas, J. D.; Liou, R.; Patel, G. F.; Perry, H. C. *J. Med. Chem.* **1988**, *31*, 2304-2315.

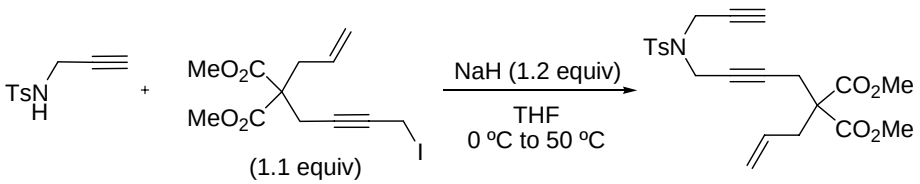
52.9 (CH_3), 39.7 (CH_2), 23.4 (CH_3), 23.1 (CH_2), 22.8 (CH_2). HRMS-ESI+ $[MH]^+$ Calc. for $C_{21}H_{27}O_8$: 407.1700; found: 407.1696.

(*E*)-Tetramethyl 2-methyl-1-phenyldodeca-1-en-6,11-diyne-4,4,9,9-tetracarboxylate (40e)



Starting from tetramethyl nona-3,8-diyne-1,1,6,6-tetracarboxylate (0.497 mmol) and (*E*)-(3-chloro-2-methylprop-1-enyl)benzene[276] (0.596 mmol) and following general procedure for alkylation (THF, 6 mL, 0ºC to 50 ºC, 17 h), **40e** was obtained in 63% yield as a pale yellowish oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34-7.16 (m, 5H), 6.41 (s, 1H), 3.75 (s, 12H), 2.99 (m, 4H), 2.94 (s, 2H), 2.85 (t, J = 2.3 Hz, 2H), 2.01 (t, J = 2.6 Hz, 1H), 1.77 (d, J = 1.3 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, DEPT-135) δ 170.8 (C), 169.4 (C), 138.1 (C), 133.0 (C), 131.0 (CH), 129.1 (CH), 128.3 (CH), 126.6 (CH), 78.8 (C), 78.0 (C), 71.7 (C), 57.5 (C), 56.8 (C), 53.2 (CH_3), 52.9 (CH_3), 42.9 (CH_2), 23.3 (CH_2), 23.2 (CH_2), 22.9 (CH_2), 18.9 (CH_3). HRMS-ESI+ $[M+Na]^+$ Calc. for $C_{27}H_{30}O_8Na$: 505.1832; found: 505.1828.

Dimethyl 2-allyl-2-(4-(4-methyl-N-(prop-2-ynyl)phenylsulfonamido)but-2-ynyl)malonate (40f)

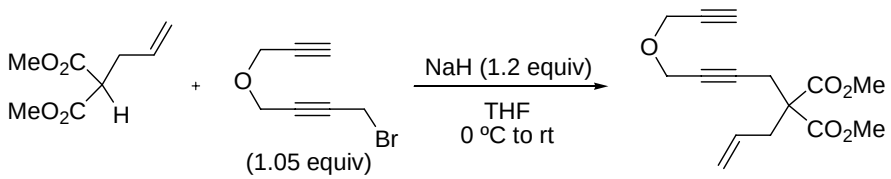


Starting from *N*-2-propynyl-(4-toluene)sulfonamide[271] (0.95 mmol) and dimethyl 2-allyl-2-(4-iodobut-2-ynyl)malonate (1.05 mmol) and following general procedure for

[276] Movassaghi, M.; Piizzi, G.; Siegel, D.S.; Pierstani, G. *Angew. Chem., Int. Ed.* **2006**, *45*, 5859-5863.

alkylation (THF, 8 mL, 0ºC to 50 ºC, 17 h), **40f** was obtained in 78% yield as a sticky yellowish oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70 (d, J = 8.2 Hz, 2H), 7.30 (d, J = 8.2 Hz, 2H), 5.61-5.46 (m, 1H), 5.14-5.05 (m, 2H), 4.12 (m, 4H), 3.71 (s, 6H), 2.67 (t, J = 2.2 Hz, 2H), 2.03 (d, J = 7.4 Hz, 2H), 2.42 (s, 3H), 2.12 (t, J = 2.5 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, DEPT-135) δ 170.3 (C), 144.0 (C), 135.6 (C), 131.8 (CH), 129.8 (CH), 128.0 (CH), 120.0 (CH_2), 81.0 (C), 76.5 (C), 75.8 (C), 74.0 (C), 57.0 (C), 52.9 (CH_3), 36.8 (CH_2), 36.7 (CH_2), 36.2 (CH_2), 23.1 (CH_2), 21.7 (CH_3). HRMS-FAB+ $[MH]^+$ Calc. for $C_{22}H_{26}NO_6S$: 432.1481; found: 432.1478.

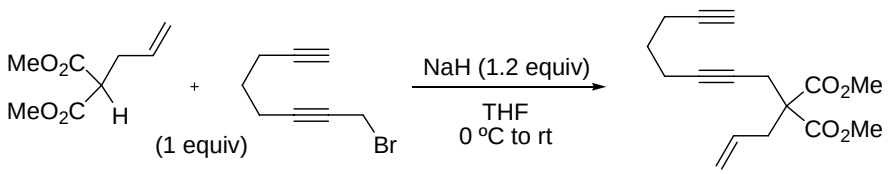
Dimethyl 2-allyl-2-(4-(prop-2-ynyloxy)but-2-ynyl)malonate (40g)



Starting from dimethyl allylmalonate (1.023 mmol, Aldrich) and 1-bromo-4-(prop-2-ynyloxy)but-2-yne[278] (1.069 mmol) and following general procedure for alkylation (THF, 8 mL, 0ºC to rt, 20 h), **40g** was obtained in 97% yield as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.69-5.54 (m, 1H), 5.21-5.09 (m, 2H), 4.21 (m, 4H), 3.73 (s, 6H), 2.84 (t, J = 2.1 Hz, 2H), 2.78 (d, J = 7.5 Hz, 2H), 2.43 (t, J = 2.3 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, DEPT-135) δ 170.4 (C), 131.9 (CH), 120.1 (CH_2), 82.1 (C), 79.2 (C), 78.5 (C), 75.0 (C), 57.2 (C), 56.9 (CH_2), 56.3 (CH_2), 52.9 (CH_3), 36.9 (CH_2), 23.3 (CH_2). HRMS-FAB+ $[MH]^+$ Calc. for $C_{15}H_{19}O_5$: 279.1232; found: 279.1230.

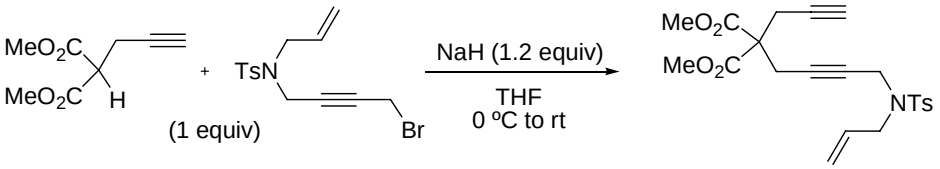
Dimethyl 2-allyl-2-(octa-2,7-diynyl)malonate (40h)

[271] Oppolzer, W.; Bedoya-Zurita, M.; Switzer, C. Y. *Tetrahedron Lett.* **1988**, *29*, 6433-6436.
[278] Griggs, R.; Scott, R.; Stevenson, P. *J. Chem. Soc., Perkin Trans. I* **1988**, 1365-1369.



Starting from dimethyl allylmalonate (0.675 mmol, Aldrich) and 8-bromoocta-1,6-diyne[279,280] (0.675) and following general procedure for alkylation (THF, 5 mL, 0ºC to rt, 20 h), **40h** was obtained in 96% yield as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.70-5.55 (m, 1H), 5.19-5.06 (m, 2H), 3.71 (s, 6H), 2.77 (d, J = 7.5 Hz, 2H), 2.75 (t, J = 2.3 Hz, 2H), 2.26 (m, 4H), 1.93 (t, J = 2.6 Hz, 1H), 1.67 (q, J = 7.0 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$, DEPT-135) δ 170.6 (C), 132.2 (CH), 119.7 (CH_2), 83.7 (C), 82.5 (C), 75.4 (C), 68.9 (C), 57.5 (C), 52.7 (CH_3), 36.9 (CH_2), 27.9 (CH_2), 23.3 (CH_2), 17.9 (CH_2), 17.6 (CH_2). HRMS-FAB+ $[MH]^+$ Calc. for $C_{16}H_{21}O_4$: 277.1440; found: 277.1437.

Dimethyl 2-(4-(*N*-allyl-4-methylphenylsulfonamido)but-2-ynyl)-2-(prop-2-ynyl)malonate (40i)

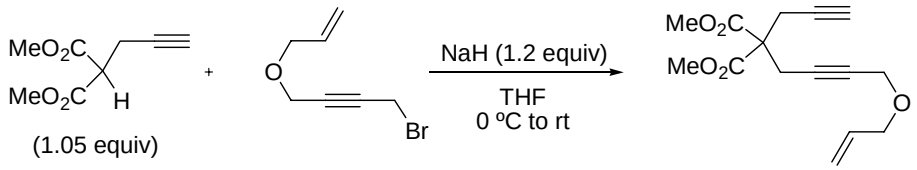


Starting from dimethyl propargylmalonate (0.876 mmol, Fluka) and *N*-allyl-*N*-(4-bromobut-2-ynyl)-4-methylbenzenesulfonamide[281] (0.876 mmol) and following general procedure for alkylation (THF, 6 mL, 0ºC to rt, 65 h), **40i** was obtained in 56% yield as a white solid (mp 66-69 ºC). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71 (d, J = 8.4 Hz, 2H), 7.32 (d, J = 8.4 Hz, 2H), 5.78-5.64 (m, 1H), 5.28 (dc, J = 17.0, 1.4 Hz, 1H), 5.22 (dd, J = 10.1, 1.2 Hz, 1H), 4.06 (t, J = 2.0 Hz, 2H), 3.77 (d, J = 7.2 Hz, 2H), 3.71 (s, 6H), 2.77 (t, J = 2.1 Hz, 2H), 2.72 (d, J = 2.7 Hz, 2H), 2.44 (s, 3H), 2.00 (t, J = 2.7 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, DEPT-135) δ 169.1 (C), 143.6 (C), 136.4 (C), 132.3 (CH), 129.7 (CH), 127.8 (CH), 120.0 (CH_2), 80.0 (C), 78.5 (C), 76.5 (C), 71.9 (C), 56.4 (C),

[279] Tanaka, R.; Nakano, Y.; Suzuki, D.; Urabe, H.; Sato, F. *J. Am. Chem. Soc* **2002**, *124*, 9682-9683.
[280] For preparation method, see procedure of **40k**. Starting from commercial available hepta-1,6-diyne.
[281] Bennacer, B.; Fujiwara, M.; Lee, S-Y.; Ojima, I. *J. Am. Chem. Soc* **2005**, *127*, 17756-17767.

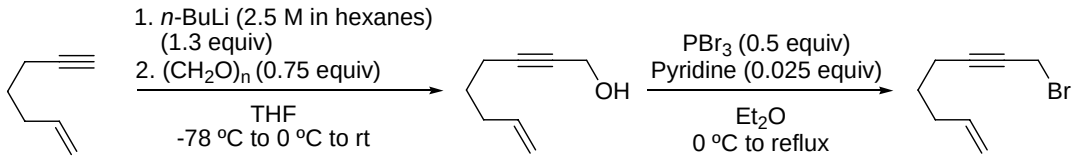
53.3 (CH_3), 49.0 (CH_2), 36.2 (CH_2), 23.0 (CH_2), 22.8 (CH_2), 21.7 (CH_3). HRMS-FAB+ $[MH]^+$ Calc. for $C_{22}H_{26}NO_6S$: 432.1481; found: 432.1473.

Dimethyl 2-(4-(allyloxy)but-2-ynyl)-2-(prop-2-ynyl)malonate (40j)



Starting from dimethyl propargylmalonate (1.11 mmol, Fluka) and 1-(allyloxy)-4-bromobut-2-yne[281] (1.06 mmol) and following general procedure for alkylation (THF, 6 mL, 0ºC to rt, 15 h), **40j** was obtained in 84% yield as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.96-5.82 (m, 1H), 5.30 (dc, J = 17.2, 1.6 Hz, 1H), 5.20 (dc, J = 10.5, 1.3 Hz, 1H), 4.11 (t, J = 2.1 Hz, 2H), 4.01 (dt, J = 5.8, 1.3 Hz, 2H), 3.75 (s, 6H), 3.04 (t, J = 2.1 Hz, 2H), 2.98 (d, J = 2.6 Hz, 2H), 2.02 (t, J = 2.6 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, DEPT-135) δ 169.3 (C), 134.2 (CH), 118.0 (CH_2), 80.8 (C), 79.7 (C), 78.6 (C), 71.9 (C), 70.5 (CH_2), 57.5 (CH_2), 56.8 (C), 53.3 (CH_3), 23.2 (CH_2), 23.0 (CH_2). HRMS-FAB+ $[MH]^+$ Calc. for $C_{15}H_{19}O_5$: 279.1232; found: 279.1229.

8-Bromooct-1-en-6-yne



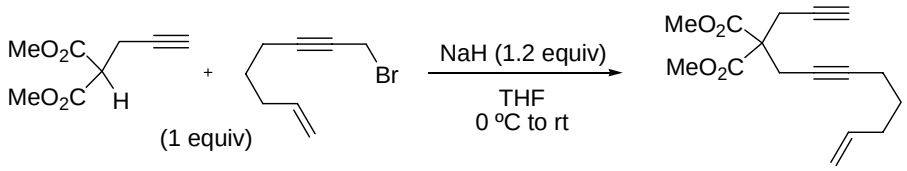
To a solution of enyne **1t** (8.50 mmol) in anhydrous THF (12 mL) at -78 ºC under Ar was added slowly a solution of *n*-BuLi (11.05 mmol, 2.5 M in hexanes). After 1 h at -78 ºC, paraformaldehyde was added and the mixture was warmed to 0 ºC for 2 h. Finally, the reaction was warmed to rt overnight. Extractive work-up with Et_2O/saturated solution of NH_4Cl, drying of the organic fractions over $MgSO_4$ and evaporation of the

[281] Bennacer, B.; Fujiwara, M.; Lee, S-Y.; Ojima, I. *J. Am. Chem. Soc* **2005**, *127*, 17756-17767.

solvent afforded the corresponding oct-7-en-2-yn-1-ol[282] as a yellowish oil without further purification.

To a solution of oct-7-en-2-yn-1-ol (3.70 mmol) in anhydrous Et_2O (15 mL) at 0 ºC was added pyridine (0.009 mmol) and then, dropwise, PBr_3 (2.70 mL, 28.38 mmol) for 10 min. After addition, the mixture was refluxed for 2 h and then was cooled to rt for 3 h. Next, a solution of $NaHCO_3$ (5%) was added carefully at 0 ºC. Extractive work-up with Et_2O, drying over $MgSO_4$, and filtration throught silica gel using pentane as eluent afforded 8-bromooct-1-en-6-yne (110 mg, 0.59 mmol) in 16% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.86-5.71 (m, 1H), 5.08-4.96 (m, 2H), 3.93 (t, J = 2.4 Hz, 2H), 2.26 (tt, J = 7.2 2.3 Hz, 2H), 2.19-2.10 (m, 4H), 1.61 (q, J = 7.2 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$, DEPT-135) δ 137.8 (CH), 115.5 (CH_2), 88.0 (C), 75.8 (C), 32.9 (CH_2), 27.7 (CH_2), 18.5 (CH_2), 15.8 (CH_2). HRMS-EI+ $[M]^+$ Calc. for $C_8H_{11}Br$: 186.0044; found: 186.0042.

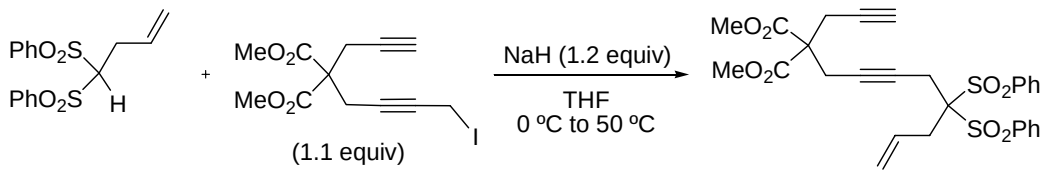
Dimethyl 2-(oct-7-en-2-ynyl)-2-(prop-2-ynyl)malonate (40k)



Starting from dimethyl propargylmalonate (0.587 mmol, Fluka) and 8-bromooct-1-en-6-yne (0.587 mmol) and following general procedure for alkylation (THF, 5 mL, 0ºC to rt, 24 h), **40k** was obtained in 43% yield as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.84-5.69 (m, 1H), 5.02 (dc, J = 17.2, 1.7 Hz, 1H), 4.99-4.94 (m, 1H), 3.74 (s, 6H), 2.97 (d, J = 2.6 Hz, 2H), 2.94 (t, J = 2.3 Hz, 2H), 2.16-2.06 (m, 4H), 2.01 (t, J = 2.6 Hz, 1H), 1.54 (q, J = 7.1 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$, DEPT-135) δ 169.5 (C), 138.0 (CH), 115.3 (CH_2), 83.8 (C), 78.8 (C), 74.3 (C), 71.6 (C), 57.0 (C), 53.1 (CH_3), 32.8 (CH_2), 28.2 (CH_2), 23.2 (CH_2), 22.9 (CH_2), 18.2 (CH_2). HRMS-ESI+ $[M+Na]^+$ Calc. for $C_{16}H_{20}O_4Na$: 299.1253; found: 299.1256.

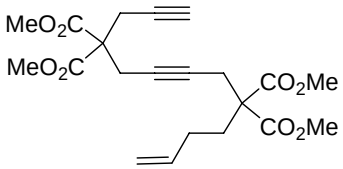
[282] Shen, K. L.; Luz, S-F.; Cheng, T-L.; Liu, R-S. *J. Org. Chem.* **2001**, *66*, 8106-8111.

Dimethyl 2-(5,5-bis(phenylsulfonyl)oct-7-en-2-ynyl)-2-(prop-2-ynyl)malonate (40l)



Starting from allyl bis(phenylsulfonyl)methane[283] (0.30 mmol, Fluka) and dimethyl 2-(4-iodobut-2-ynyl)-2-(prop-2-ynyl)malonate (0.33 mmol) and following general procedure for alkylation (THF, 5 mL, 0ºC to 50 ºC, 16 h), **40l** was obtained in 33% yield as a sticky yellowish oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.10 (d, J = 7.4 Hz, 4H), 7.70 (t, J = 7.7 Hz, 2H), 7.58 (t, J = 7.7 Hz, 4H), 6.11-5.96 (m, 1H), 5.35-5.25 (m, 2H), 3.74 (s, 6H), 3.10 (t, J = 2.3 Hz, 2H), 3.06 (d, J = 6.6 Hz, 2H), 3.02 (d, J = 2.7 Hz, 2H), 2.94 (t, J = 2.2 Hz, 2H), 2.04 (t, J = 2.7 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, DEPT-135) δ 169.3 (C), 136.9 (C), 134.9 (CH), 131.8 (CH), 130.0 (CH), 128.7 (CH), 121.0 (CH_2), 89.2 (C), 80.6 (C), 78.9 (C), 75.4 (C), 71.8 (C), 56.6 (C), 53.3 (CH_3), 33.3 (CH_2), 23.4 (CH_2), 23.0 (CH_2), 21.3 (CH_2). HRMS-FAB+ $[MH]^+$ Calc. for $C_{28}H_{29}O_8S_2$: 557.1304; found: 557.1294.

Tetramethyl trideca-12-en-1,6-diyne-4,4,9,9-tetracarboxylate (47)

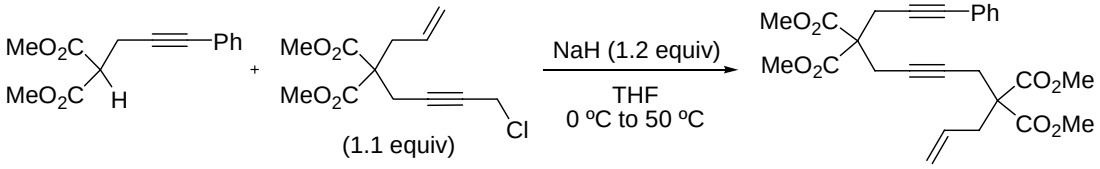


Starting from tetramethyl nona-3,8-diyne-1,1,6,6-tetracarboxylate (0.568 mmol) and 4-bromobut-1-ene (0.681 mmol, Aldrich) and following general procedure for alkylation (THF, 5 mL, 0ºC to 50 ºC, 20 h), **47** was obtained in 61% yield as a pale yellowish oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.86-5.71 (m, 1H), 5.05 (dc, J = 17.2, 1.6 Hz, 1H), 4.98 (dc, J = 10.3, 1.5 Hz, 1H), 3.74 (s, 6H), 3.72 (s, 6H), 2.95-2.92 (m, 4H), 2.79 (t, J = 2.3 Hz, 2H), 2.13-2.05 (m, 2H), 2.00 (t, J = 2.7 Hz, 1H), 1.98-1.88 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$, DEPT-135) δ 170.8 (C), 169.3 (C), 137.5 (CH), 115.4 (CH_2), 78.7 (C),

[283] Du Penhoat, H. C.; Julia, M. *Tetrahedron* **1986**, *42*, 4807-4816.

78.2 (C), 77.4 (C), 71.7 (C), 56.9 (C), 56.7 (C), 53.2 (CH_3), 52.9 (CH_3), 31.4 (CH_2), 28.5 (CH_2), 23.3 (CH_2), 23.1 (CH_2), 22.8 (CH_2). HRMS-ESI+ $[MH]^+$ Calc. for $C_{21}H_{27}O_8$: 407.1700; found: 407.1701.

Tetramethyl 12-phenyldodeca-1-en-6,11-diyne-4,4,9,9-tetracarboxylate (51)



Starting from dimethyl 2-(3-phenylprop-2-ynyl)malonate[261] (0.61 mmol) and 2-allyl-2-(4-chlorobut-2-ynyl)malonate (0.67 mmol, Aldrich) and following general procedure for alkylation (THF, 5 mL, 0ºC to 50 ºC, 70 h), **51** was obtained in 35% yield as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38-7.34 (m, 2H), 7.29-7.25 (m, 3H), 5.69-5.54 (m, 1H), 5.22-5.08 (m, 2H), 3.78 (s, 6H), 3.74 (s, 6H), 3.17 (s, 2H), 3.02 (t, J = 2.3 Hz, 2H), 2.80-2.75 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$, DEPT-135) δ 170.4 (C), 169.5 (C), 132.1 (CH), 131.9 (CH), 128.4 (CH), 128.2 (CH), 123.4 (C), 119.9 (CH_2), 84.2 (C), 83.9 (C), 78.3 (C), 77.8 (C), 57.3 (C), 57.2 (C), 53.2 (CH_3), 52.8 (CH_3), 36.8 (CH_2), 23.8 (CH_2), 23.4 (CH_2), 23.2 (CH_2). HRMS-FAB+ $[MH]^+$ Calc. for $C_{26}H_{29}O_8$: 469.1862; found: 469.1859.

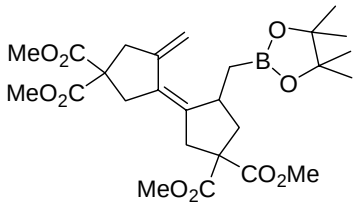
4.2 General optimized procedure for the synthesis of allylboronates from 6-ene-1,11-diynes

The corresponding endiyne (*ca.* 50 mg), bis(pinacolato)diboron (1.2 equiv), and $Pd(OAc)_2$ (5 mol%) were sequentially added to a 5 mL flask. After purging with Ar, dry toluene (1 mL) and MeOH (1 equiv) were added. The mixture was heated at 50ºC for the indicated time. After cooling to room temperature, Celite® was added and solvent was evaporated. Column chromatography (hexane/EtOAc) afforded the product. To obtain the highest possible yield, a 2 cm diameter column filled with 8-12 cm height of silicagel was used. Partial decomposition of the boronate was detected when using longer columns or retention times, probably due to hydrolysis.

[261] Schiller, R.; Pour, M.; Fakova, H.; Kunes, J.; Cisarova, I. *J. Org. Chem.* **2004**, *69*, 6761-6765.

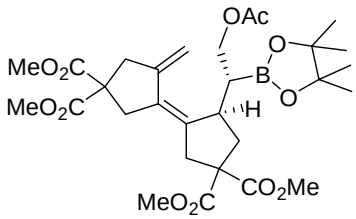
4.2.1 Experimental data of alkylboronates

Tetramethyl (1*Z*)-5-methylene-5'-[(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl]-1,1'-bi(cyclopentylidene)-3,3,3',3'-tetracarboxylate (41a)



Following general borylative polycyclization procedure, **41a** was obtained after 2 h in 60% yield (71% yield when was scaled up to 400 mg of enediyne) as a colorless oil (hexane/EtOAc 6:1 to 4:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.08 (s, 1H), 5.02 (s, 1H), 3.73 (s, 3H), 3.71 (s, 6H), 3.70 (s, 3H), 3.27-2.78 (m, 7H), 2.67 (dd, J = 13.5, 8.4 Hz, 1H), 2.12 (dd, J = 13.5, 4.5 Hz, 1H), 1.22 (br s, 13H), 0.71 (dd, J = 16.3, 11.5 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.7 (C), 172.5 (C), 172.0 (C), 171.9 (C), 143.8 (C), 143.2 (C), 127.3 (C), 109.7 (CH_2), 83.2 (C), 58.6 (C), 57.5 (C), 53.0 (CH_3), 52.9 (CH_3), 43.6 (CH_2), 41.8 (CH_2), 40.9 (CH_2), 40.8 (CH_2), 36.7 (CH), 25.0 (CH_3), 24.9 (CH_3), 15.4 (CH_2-B, HMQC). HRMS-ESI+ $[M+Na]^+$ Calc. for $C_{26}H_{37}BO_{10}Na$: 543.2371; found: 543.2355.

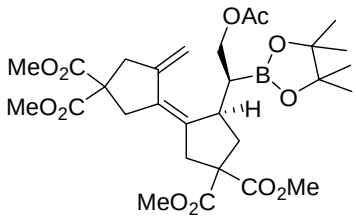
(*rac*)-Tetramethyl (1*Z*,5*R*)-5-[(1*R*)-2-(acetyloxy)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl]-5'-methylene-1,1'-bi(cyclopentylidene)-3,3,3',3'-tetracarboxylate (41b)



Following general borylative polycyclization procedure, **41b** was obtained after 22 h in 66% yield as a colorless oil (hexane/EtOAc 5:1 to 3:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.13 (s, 1H), 5.10 (s, 1H), 4.22 (dd, J = 11.1, 5.5 Hz, 1H), 4.05 (dd, J = 10.8, 9.8 Hz, 1H), 3.73 (s, 3H), 3.71 (s, 6H), 3.70 (s, 3H), 3.30 (m, 1H), 3.22-2.77 (m, 6H), 2.70 (ddd,

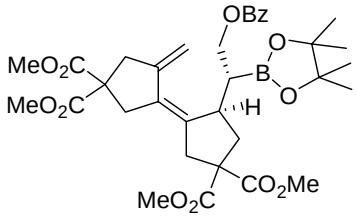
J = 13.4, 8.4, 1.3 Hz, 1H), 2.27 (q, *J* = 4.8 Hz, 1H), 2.15 (dd, *J* = 13.2, 8.0 Hz, 1H), 2.02 (s, 3H), 1.19 (s, 12H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.3 (C), 172.1 (C), 172.0 (C), 171.9 (C), 171.3 (C), 143.9 (C), 140.5 (C), 128.7 (C), 110.3 (CH_2), 83.6 (C), 65.1 (CH_2), 58.8 (C), 57.3 (C), 53.0 (CH_3), 52.9 (CH_3), 52.8 (CH_3), 43.8 (CH_2), 41.8 (CH_2), 41.4 (CH_2), 38.8 (CH_2), 38.5 (CH), 25.4 (CH-B, HMQC), 25.0 (CH_3), 24.9 (CH_3), 21.1 (CH_3). HRMS-ESI+ $[M+Na]^+$ Calc. for $C_{29}H_{41}BO_{12}Na$: 615.2583; found: 615.2577.

(*rac*)-Tetramethyl (1*Z*,5*R*)-5-[(1*S*)-2-(acetyloxy)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl]-5'-methylene-1,1'-bi(cyclopentylidene)-3,3,3',3'-tetracarboxylate (41b')



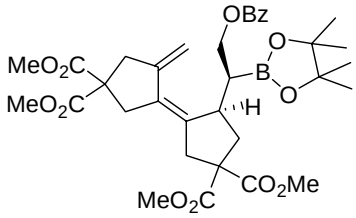
Following general borylative polycyclization procedure, **41b'** was obtained after 6 h in 30% yield as a colorless oil (hexane/EtOAc 4:1 to 2:1) as a diastereomer of **41b**. This compound was difficult to purify since decomposed to **42**. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.15 (s, 1H), 5.09 (s, 1H), 4.21 (dd, *J* = 11.1, 6.4 Hz, 1H), 4.03 (dd, *J* = 11.1, 7.2 Hz, 1H), 3.74 (s, 3H), 3.71 (s, 9H), 3.41 (m, 1H), 3.13-2.93 (m, 4H), 2.86 (d, *J* = 15.1 Hz, 2H), 2.65 (dd, *J* = 13.6, 9.1 Hz, 1H), 2.22 (m, 2H), 1.98 (s, 3H), 1.21 (s, 6H), 1.20 (s, 6H). HRMS-ESI+ $[M+Na]^+$ Calc. for $C_{29}H_{41}BO_{12}Na$: 615.2583; found: 615.2571.

(*rac*)-Tetramethyl (1*Z*,5*R*)-5-[(1*R*)-2-(benzoyloxy)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl]-5'-methylene-1,1'-bi(cyclopentylidene)-3,3,3',3'-tetracarboxylate (41c)



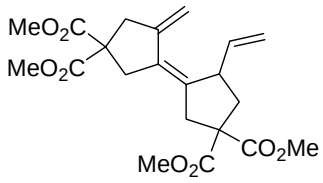
Following general borylative polycyclization procedure, **41c** was obtained after 23 h in 70% yield as a sticky colorless oil (hexane/EtOAc 3:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.02 (d, J = 7.6 Hz, 2H), 7.54 (t, J = 7.5 Hz, 1H), 7.42 (t, J = 7.5 Hz, 2H), 5.16 (s, 1H), 5.12 (s, 1H), 4.47 (dd, J = 11.1, 5.1 Hz, 1H), 4.33 (dd, J = 10.6, 9.6 Hz, 1H), 3.74 (s, 3H), 3.72 (s, 3H), 3.71 (s, 3H), 3.69 (s, 3H), 3.44 (m, 1H), 3.25-2.72 (m, 7H), 2.44 (q, J = 4.8 Hz, 1H), 2.25 (dd, J = 13.3, 7.9 Hz, 1H), 1.19 (s, 12H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.3 (C), 172.1 (C), 172.0 (C), 171.9 (C), 166.8 (C), 143.9 (C), 140.5 (C), 132.9 (CH), 130.6 (C), 129.7 (CH), 128.8 (C), 128.4 (CH), 110.5 (CH_2), 83.6 (C), 65.7 (CH_2), 58.8 (C), 57.3 (C), 53.0 (CH_3), 52.9 (CH_3), 52.8 (CH_3), 43.8 (CH_2), 41.8 (CH_2), 41.4 (CH_2), 38.9 (CH_2), 38.7 (CH), 25.5 (CH-B, HMQC), 25.1 (CH_3), 25.0 (CH_3). HRMS-ESI+ $[M+Na]^+$ Calc. for $C_{34}H_{43}BO_{12}Na$: 677.2739; found: 677.2731.

(*rac*)-Tetramethyl (1*Z*,5*R*)-5-[(1*S*)-2-(benzoyloxy)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl]-5'-methylene-1,1'-bi(cyclopentylidene)-3,3,3',3'-tetracarboxylate (41c')



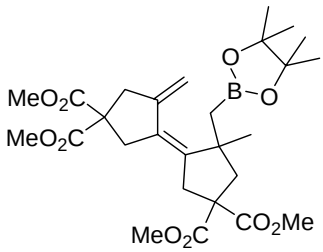
Following general borylative polycyclization procedure, **41c'** was obtained after 21 h in 25% yield as a sticky colorless oil (hexane/EtOAc 4:1 to 2:1) as a diastereomer of **41c**. This compound was difficult to purify since decomposed to **42**. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.97 (d, J = 8.2 Hz, 2H), 7.52 (t, J = 7.4 Hz, 1H), 7.41 (t, J = 7.3 Hz, 2H), 5.16 (s, 1H), 5.13 (s, 1H), 4.47 (dd, J = 11.4, 5.8 Hz, 1H), 4.34 (dd, J = 11.4, 7.5 Hz, 1H), 3.71 (s, 3H), 3.70 (s, 3H), 3.69 (s, 3H), 3.65 (s, 3H), 3.49 (m, 1H), 3.10-2.95 (m, 4H), 2.86 (d, J = 16.4 Hz, 1H), 2.72 (ddd, J = 13.7, 8.8, 1.3 Hz, 1H), 2.68 (d, J = 17.6 Hz, 1H), 2.45 (m, 1H), 2.30 (dd, J = 13.7, 7.9 Hz, 1H), 1.20 (s, 12H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.1 (C), 171.8 (C), 166.6 (C), 143.6 (C), 140.3 (C), 132.9 (CH), 130.7 (C), 129.7 (CH), 128.7 (C), 128.5 (CH), 110.8 (CH_2), 83.8 (C), 63.9 (CH_2), 58.6 (C), 53.0 (CH_3), 52.9 (CH_3), 52.8 (CH_3), 43.7 (CH_2), 42.3 (CH_2), 41.2 (CH_2), 38.9 (CH), 37.1 (CH_2), 25.0 (CH_3), 24.9 (CH_3), 23.7 (CH-B, HMQC). HRMS-ESI+ $[M+Na]^+$ Calc. for $C_{34}H_{43}BO_{12}Na$: 677.2739; found: 677.2739.

Tetramethyl (1*Z*)-5-methylene-5'-vinyl-1,1'-bi(cyclopentylidene)-3,3,3',3'-tetracarboxylate (42)



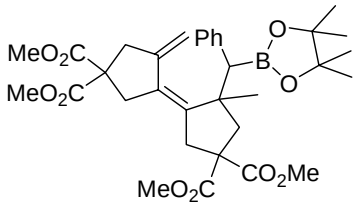
Following general borylative polycyclization procedure, **42** was obtained by decomposition of **41b'** an **41c'** in variable quantities as a sticky white solid. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.63 (ddd, J = 17.2, 10.3, 5.0 Hz, 1H), 5.03 (s, 2H), 4.98 (dt, J = 10.3, 1.5 Hz, 1H), 4.89 (dt, J = 17.2, 1.5 Hz, 1H), 3.73 (s, 6H), 3.72 (s, 3H), 3.69 (s, 3H), 3.59 (m, 1H), 3.21 (d, J = 17.3 Hz, 1H), 3.01 (m, 4H), 2.84 (d, J = 17.3 Hz, 1H), 2.62 (dd, J = 13.1, 8.5 Hz, 1H), 2.39 (dd, J = 13.1, 2.9 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 172.4, 172.0, 171.9, 143.7, 137.4, 137.0, 130.7, 115.4, 110.5, 58.5, 57.6, 53.1, 53.0, 52.9, 45.3, 43.2, 41.0, 40.9, 40.7.

Tetramethyl (1*Z*)-5-methyl-5'-methylene-5-[(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl]-1,1'-bi(cyclopentylidene)-3,3,3',3'-tetracarboxylate (41d)



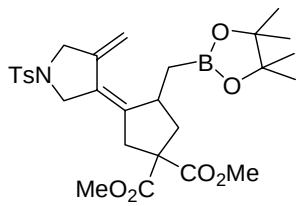
Following general borylative polycyclization procedure, **41d** was obtained after 4 h in 81% yield as a white solid (hexane/EtOAc 3:1 to 2.5:1), mp 105-108 ºC. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.15 (s, 1H), 5.12 (s, 1H), 3.74 (s, 3H), 3.72 (s, 6H), 3.71 (s, 3H), 3.16-2.77 (m, 6H), 2.67 (d, J = 13.5 Hz, 1H), 2.40 (dd, J = 13.5, 1.3 Hz, 1H), 1.33 (m, 2H), 1.23 (s, 3H), 1.20 (s, 6H), 1.19 (s, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 173.0 (C), 172.8 (C), 172.2 (C), 172.1 (C), 145.4 (C), 143.7 (C), 128.4 (C), 112.6 (CH_2), 83.0 (C), 57.8 (C), 56.5 (C), 53.0 (CH_3), 52.9 (CH_3), 50.6 (CH_2), 44.1 (CH_2), 44.0 (C), 42.7 (CH_2), 41.4 (CH_2), 28.3 (CH_3), 25.1 (CH_3), 24.9 (CH_3), 22.2 (CH_2-B, HMQC). HRMS-ESI+ $[M+Na]^+$ Calc. for $C_{27}H_{39}BO_{10}Na$: 557.2528; found: 557.2527.

Tetramethyl (1*Z*)-5-methyl-5'-methylene-5-[phenyl(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl]-1,1'-bi(cyclopentylidene)-3,3,3',3'-tetracarboxylate (41e)



Following general borylative polycyclization procedure, **41e** was obtained after 3.5 h in 80% yield as a colorless oil (hexane/EtOAc 2.5:1 to 2:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.25-7.10 (m, 5H), 5.50 (s, 1H), 5.29 (s, 1H), 3.75 (s, 3H), 3.72 (s, 3H), 3.71 (s, 3H), 3.61 (s, 3H), 3.31 (s, 1H), 3.10-2.72 (m, 7H), 2.50 (dd, *J* = 14.3, 2.2 Hz, 1H), 1.40 (s, 3H), 1.27 (s, 3H), 1.22 (s, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.9 (C), 172.1 (C), 172.0 (C), 145.2 (C), 143.9 (C), 139.6 (C), 131.4 (CH), 128.9 (C), 127.8 (CH), 126.0 (CH), 113.5 (CH_2), 83.6 (C), 57.7 (C), 56.5 (C), 52.9 (CH_3), 52.8 (CH_3), 52.7 (CH_3), 48.5 (C), 45.7 (CH_2), 44.9 (CH_2), 43.9 (CH_2), 42.6 (CH_2), 38.3 (CH-B, HMQC), 26.4 (CH_3), 25.0 (CH_3), 24.9 (CH_3). HRMS-ESI+ $[M+Na]^+$ Calc. for $C_{33}H_{43}BO_{10}Na$: 633.2841; found: 633.2835.

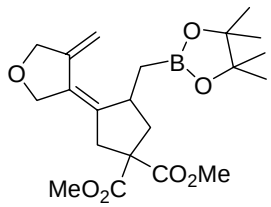
Dimethyl (1*Z*)-2'-methylene-4'-[(4-methylphenyl)sulfonyl]-5-[(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl]-1,1'-bi(cyclopentylidene)-3,3-dicarboxylate (41f)



Following general borylative polycyclization procedure, **41f** was obtained after 18 h in 44% yield as a colorless oil (hexane/EtOAc 4:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.1 Hz, 2H), 7.32 (d, *J* = 8.1 Hz, 2H), 5.06 (s, 1H), 5.04 (s, 1H), 3.94 (m, 2H), 3.88 (m, 1H), 3.82 (m, 1H), 3.74 (s, 3H), 3.69 (s, 3H), 3.13 (m, 1H), 3.07 (d, *J* = 17.5 Hz, 1H), 2.75-2.58 (m, 2H), 2.42 (s, 3H), 2.13 (dd, *J* = 13.4, 4.7 Hz, 1H), 1.20 (s, 6H), 1.19 (s, 6H), 1.10 (dd, *J* = 16.5, 2.8 Hz, 1H), 0.66 (dd, *J* = 16.5, 11.4 Hz, 1H). ^{13}C-NMR (75

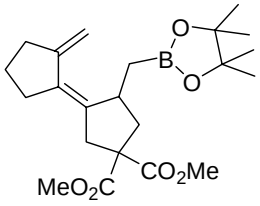
MHz, $CDCl_3$, DEPT-135) δ 172.3 (C), 172.2 (C), 143.9 (C), 143.8 (C), 140.2 (C), 133.0 (C), 129.9 (CH), 128.1 (CH), 124.5 (C), 109.3 (CH_2), 83.4 (C), 58.6 (C), 55.0 (CH_2), 53.3 (CH_2), 53.0 (CH_3), 41.6 (CH_2), 40.6 (CH_2), 36.8 (CH), 25.0 (CH_3), 24.8 (CH_3), 21.7 (CH_3), 14.6 (CH_2-B, HMQC). HRMS-ESI+ $[MH]^+$ Calc. for $C_{28}H_{39}BNO_8S$: 560.2483; found: 560.2486.

Dimethyl (3*E*)-3-(4-methylenedihydrofuran-3(2*H*)-ylidene)-4-[(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl]cyclopentane-1,1-dicarboxylate (41g)



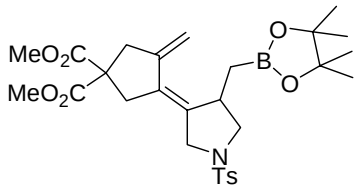
Following general borylative polycyclization procedure, **41g** was obtained after 22 h in 14% yield as a colorless oil (hexane/EtOAc 3.5:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.09 (s, 1H), 5.06 (s, 1H), 4.45 (m, 2H), 4.43-4.35 (m, 2H), 3.74 (s, 3H), 3.70 (s, 3H), 3.24 (m, 1H), 3.08 (m, 1H), 2.77-2.66 (m, 2H), 2.15 (dd, J = 13.6, 4.8 Hz, 1H), 1.29 (m, 1H), 1.24 (s, 12H), 0.77 (dd, J = 16.3, 11.4 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.5 (C), 172.3 (C), 143.3 (C), 141.1 (C), 127.3 (C), 106.2 (CH_2), 83.4 (C), 74.8 (CH_2), 73.3 (CH_2), 59.0 (C), 53.1 (CH_3), 53.0 (CH_3), 41.6 (CH_2), 40.2 (CH_2), 36.6 (CH), 25.0 (CH_3), 24.9 (CH_3), 15.2 (CH_2-B, HMQC). HRMS-ESI+ $[M+Na]^+$ Calc. for $C_{21}H_{31}BO_7Na$: 429.2055; found: 429.2044.

Dimethyl (1*Z*)-2'-methylene-5-[(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl]-1,1'-bi(cyclopentylidene)-3,3-dicarboxylate (41h)



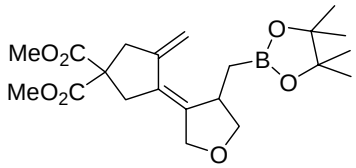
Following general borylative polycyclization procedure, **41h** was obtained after 5 h in 30% yield (calculated by NMR) as a colorless oil (hexane/EtOAc 10:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.05 (s, 1H), 4.97 (s, 1H), 3.75 (s, 3H), 3.70 (s, 3H), 3.24 (m, 1H), 3.12 (d, J = 16.8 Hz, 1H), 2.83 (d, J = 16.8 Hz, 1H), 2.67 (dd, J = 13.4, 8.2 Hz, 1H), 2.39 (m, 2H), 2.32 (m, 2H), 2.17 (dd, J = 13.2, 4.2 Hz, 1H), 1.64 (q, J = 7.2 Hz, 2H), 1.29 (m, 1H), 1.23 (s, 12H), 0.74 (dd, J = 16.2, 11.6 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 173.0 (C), 172.8 (C), 148.4 (C), 141.2 (C), 131.1 (C), 107.8 (CH_2), 83.2 (C), 58.6 (C), 52.9 (CH_3), 42.0 (CH_2), 40.0 (CH_2), 37.1 (CH_2), 36.7 (CH), 33.9 (CH_2), 25.1 (CH_3), 24.8 (CH_3), 23.0 (CH_2), 15.5 (CH_2-B, HMQC). HRMS-ESI+ $[MH]^+$ Calc. for $C_{22}H_{34}BO_6$: 405.2442; found: 405.2438.

Dimethyl (1*Z*)-5-methylene-4'-[(4-methylphenyl)sulfonyl]-2'-[(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl]-1,1'-bi(cyclopentylidene)-3,3-dicarboxylate (41i)



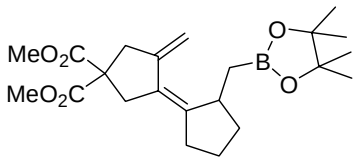
Following general borylative polycyclization procedure, **41i** was obtained after 15 h in 51% yield as a white solid (hexane/EtOAc 4:1), mp 117-120 ºC. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.72 (d, J = 8.1 Hz, 2H), 7.33 (d, J = 8.1 Hz, 2H), 5.08 (s, 1H), 5.00 (s, 1H), 3.99 (d, J = 15.2 Hz, 1H), 3.72 (s, 3H), 3.68 (s, 3H), 3.50 (d, J = 15.2 Hz, 1H), 3.37 (d, J = 8.7 Hz, 1H), 3.15 (m, 1H), 3.07 (dd, J = 9.0, 6.0 Hz, 1H), 2.98 (m, 2H), 2.79 (s, 2H), 2.43 (s, 3H), 1.22 (s, 12H), 1.02 (d, J = 2.2 Hz, 1H), 0.99 (s, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 171.8 (C), 171.6 (C), 143.8 (C), 143.7 (C), 138.7 (C), 132.7 (C), 129.8 (CH), 128.2 (CH), 127.2 (C), 110.0 (CH_2), 83.5 (C), 57.6 (C), 55.5 (CH_2), 53.1 (CH_3), 53.0 (CH_3), 52.1 (CH_2), 43.2 (CH_2), 40.2 (CH_2), 37.0 (CH), 25.0 (CH_3), 21.7 (CH_3), 14.7 (CH_2-B, HMQC). HRMS-FAB+ $[MH]^+$ Calc. for $C_{28}H_{39}BNO_8S$: 560.2489; found: 560.2472.

Dimethyl (4*E*)-3-methylene-4-[4-[(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl]dihydrofuran-3(2*H*)-ylidene]cyclopentane-1,1-dicarboxylate (41j)



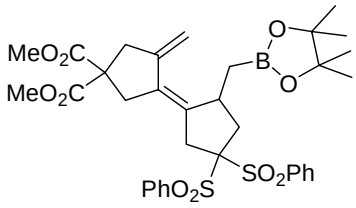
Following general borylative polycyclization procedure, **41j** was obtained after 14.5 h in 41% yield as a colorless oil (hexane/EtOAc 5:1 to 4:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.13 (s, 1H), 5.10 (s, 1H), 4.41 (d, J = 14.7 Hz, 1H), 4.19 (d, J = 14.7 Hz, 1H), 3.82 (d, J = 3.0 Hz, 2H), 3.72 (s, 6H), 3.17 (m, 1H), 3.04 (br s, 2H), 2.83 (m, 2H), 1.23 (s, 12H), 1.10-0.99 (m, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 171.9 (C), 171.8 (C), 144.1 (C), 142.2 (C), 124.7 (C), 108.9 (CH_2), 83.4 (C), 75.9 (CH_2), 71.4 (CH_2), 57.9 (C), 53.0 (CH_3), 43.0 (CH_2), 40.0 (CH_2), 38.0 (CH), 25.0 (CH_3), 24.9 (CH_3), 13.7 (CH_2-B, HMQC). HRMS-ESI+ $[MH]^+$ Calc. for $C_{21}H_{32}BO_7$: 407.2235; found: 407.2224.

Dimethyl (1*Z*)-5-methylene-2'-[(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl]-1,1'-bi(cyclopentylidene)-3,3-dicarboxylate (41k)



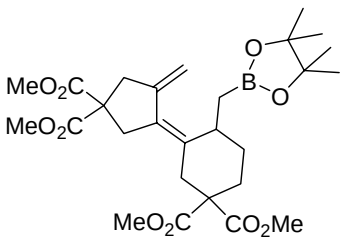
Following general borylative polycyclization procedure, **41k** was obtained after 3.5 h in 64% yield (calculated by NMR) as a colorless oil (hexane/EtOAc 10:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.12 (s, 1H), 5.03 (s, 1H), 3.71 (s, 6H), 3.09 (m, 1H), 3.03 (t, J = 1.8 Hz, 2H), 2.91 (m, 2H), 2.42-2.12 (m, 2H), 1.82-1.51 (m, 4H), 1.24 (s, 6H), 1.23 (s, 6H), 1.06 (dd, J = 15.9, 2.0 Hz, 1H), 0.74 (dd, J = 15.9, 11.9 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.3 (C), 172.2 (C), 148.5 (C), 144.4 (C), 125.5 (C), 108.0 (CH_2), 83.2 (C), 57.6 (C), 52.9 (CH_3), 43.8 (CH_2), 41.0 (CH_2), 37.7 (CH), 34.7 (CH_2), 33.2 (CH_2), 25.0 (CH_3), 24.9 (CH_3), 22.7 (CH_2), 14.5 (CH_2-B, HMQC). HRMS-ESI+ $[M+Na]^+$ Calc. for $C_{22}H_{33}BO_6Na$: 427.2262; found: 427.2262.

Dimethyl (1*Z*)-5-methylene-4',4'-bis(phenylsulfonyl)-2'-[(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl]-1,1'-bi(cyclopentylidene)-3,3-dicarboxylate (41l)



Following general borylative polycyclization procedure, **41l** was obtained after 24 h in 54% yield as a colorless oil (hexane/EtOAc 3:1 to 2.5:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.12 (m, 2H), 7.97 (m, 2H), 7.76-7.50 (m, 6H), 5.09 (s, 1H), 4.79 (s, 1H), 3.77 (s, 3H), 3.72 (s, 3H), 3.62 (m, 1H), 3.07-2.85 (m, 6H), 2.73 (m, 1H), 2.54 (dd, J = 15.1, 6.0 Hz, 1H), 1.28 (m, 1H), 1.23 (s, 6H), 1.22 (s, 6H), 0.91 (dd, J = 16.0, 10.7 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 171.8 (C), 143.3 (C), 140.8 (C), 137.7 (C), 136.3 (C), 134.7 (CH), 134.6 (CH), 131.4 (CH), 131.1 (CH), 129.0 (CH), 128.8 (CH), 128.0 (C), 111.1 (CH_2), 92.5 (C), 83.4 (C), 57.4 (C), 53.1 (CH_3), 53.0 (CH_3), 43.7 (CH_2), 41.1 (CH_2), 39.4 (CH_2), 38.4 (CH_2), 37.2 (CH), 25.1 (CH_3), 25.0 (CH_3), 15.6 (CH_2-B, HMQC). HRMS-ESI+ $[M+Na]^+$ Calc. for $C_{34}H_{41}BO_{10}S_2Na$: 707.2126; found: 707.2138.

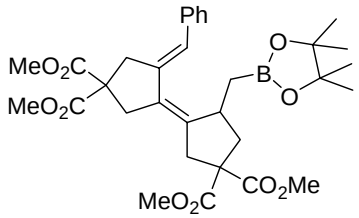
Dimethyl (3*Z*)-3-[4,4-bis(methoxycarbonyl)-2-methylenecyclopentylidene]-4-[(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl]cyclohexane-1,1-dicarboxylate (48)



Following general borylative polycyclization procedure, **48** was obtained after 4 h in 78% yield as a cristalline white solid (hexane/EtOAc 3:1), mp 109-112 ºC. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.18 (s, 1H), 5.07 (s, 1H), 3.73 (s, 3H), 3.71 (s, 3H), 3.70 (s, 6H), 3.40 (m, 1H), 3.24-2.85 (m, 5H), 2.55 (d, J = 14.6 Hz, 1H), 2.21-1.99 (m, 2H), 1.72-1.49 (m, 2H), 1.25 (m, 1H), 1.21 (s, 6H), 1.20 (s, 6H), 0.88 (dd, J = 15.5, 4.6 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.6 (C), 172.2 (C), 171.2 (C), 144.5 (C),

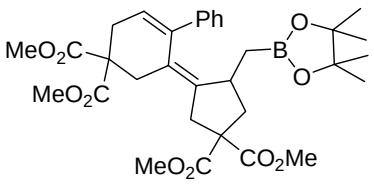
137.0 (C), 129.7 (C), 110.6 (CH_2), 83.2 (C), 56.7 (C), 56.6 (C), 52.9 (CH_3), 52.8 (CH_3), 52.5 (CH_3), 43.8 (CH_2), 38.8 (CH_2), 32.2 (CH_2), 32.0 (CH), 28.5 (CH_2), 25.9 (CH_2), 25.1 (CH_3), 24.9 (CH_3), 14.4 (CH_2-B, HMQC). HRMS-ESI+ $[MH]^+$ Calc. for $C_{27}H_{40}BO_{10}$: 537.2709; found: 537.2720.

Tetramethyl (1*Z*,5*E*)-5-benzylidene-5'-[(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl]-1,1'-bi(cyclopentylidene)-3,3,3',3'-tetracarboxylate (52)



Following general borylative polycyclization procedure, **52** was obtained after 18 h in a mixture with **53** (65% yield calculated by NMR; **52**:**53** (60:40)) and 12% isolated yield as a sticky colorless oil (hexane/EtOAc 6:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.76-7.28 (m, 4H), 7.23-7.16 (m, 1H), 6.59 (s, 1H), 3.76 (s, 3H), 3.73 (s, 3H), 3.70 (s, 3H), 3.69 (s, 3H), 3.39 (m, 1H), 3.31 (s, 2H), 3.18 (d, J = 17.4 Hz, 1H), 3.03-2.87 (m, 3H), 2.72 (dd, J = 13.4, 8.2 Hz, 1H), 2.15 (dd, J = 13.4, 5.0 Hz, 1H), 1.35 (dd, J = 16.2, 2.6 Hz, 1H), 1.22 (s, 6H), 1.21 (s, 6H), 0.80 (dd, J = 16.2, 11.4 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.7 (C), 172.1 (C), 142.0 (C), 138.4 (C), 137.6 (C), 129.7 (C), 129.1 (CH), 128.3 (CH), 126.7 (CH), 126.0 (CH), 83.3 (C), 58.5 (C), 58.0 (C), 53.0 (CH_3), 52.9 (CH_3), 42.0 (CH_2), 41.5 (CH_2), 40.4 (CH_2), 40.2 (CH_2), 37.0 (CH), 25.1 (CH_3), 24.9 (CH_3), 15.8 (CH_2-B, HMQC). HRMS-ESI+ $[M+Na]^+$ Calc. for $C_{32}H_{41}BO_{10}Na$: 619.2684; found: 619.2694.

Dimethyl (5*Z*)-5-{4,4-bis(methoxycarbonyl)-2-[(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl]cyclopentylidene}-4-phenylcyclohex-3-ene-1,1-dicarboxylate (53)

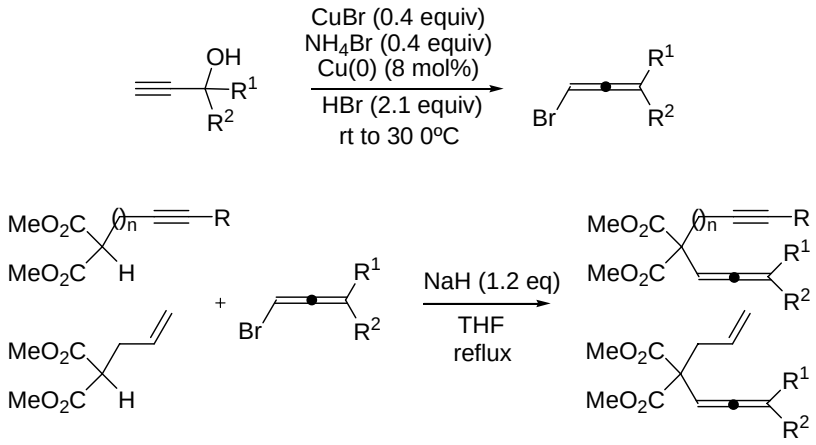


Following general borylative polycyclization procedure, **53** was obtained after 18 h in a mixture with **52** (65% yield calculated by NMR; **52**:**53** (60:40)) and 12% isolated yield as a sticky colorless oil (hexane/EtOAc 6:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.33-7.27 (m, 4H), 7.21-7.13 (m, 1H), 6.08 (q, J = 2.5 Hz, 1H), 3.74 (s, 6H), 3.72 (s, 3H), 3.70 (m, 1H), 3.65 (s, 3H), 3.43 (d, J = 17.8 Hz, 1H), 3.20-3.10 (m, 2H), 3.01 (d, J = 16.4 Hz, 1H), 2.92 (d, J = 3.8 Hz, 2H), 2.51 (ddd, J = 12.7, 7.2, 1.6 Hz, 1H), 2.04 (t, J = 12.7, 1H), 1.79 (d, J = 14.9 Hz, 1H), 1.68 (d, J = 14.9 Hz, 1H), 1.22 (s, 12H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.9 (C), 172.7 (C), 172.2 (C), 141.6 (C), 138.2 (C), 133.5 (C), 130.5 (C), 128.5 (CH), 128.4 (CH), 126.3 (CH), 123.4 (CH), 83.6 (C), 59.7 (C), 57.7 (C), 53.1 (CH_3), 53.0 (CH_3), 52.9 (CH_3), 52.8 (CH_3), 45.6 (CH_2), 43.8 (CH), 39.7 (CH_2), 39.0 (CH_2), 37.4 (CH_2), 25.0 (CH_3), 24.9 (CH_3), 12.7 (CH_2-B, HMQC). HRMS-ESI+ $[M+Na]^+$ Calc. for $C_{32}H_{41}BO_{10}Na$: 619.2684; found: 619.2699.

5. Pd-Catalyzed Borylative Cyclization of Allenynes and Enallenes

5.1 Preparation of allenynes and enallenes

Next scheme show the general procedure for the preparation of allenynes and enallenes:



Bromoallenes were prepared from the corresponding disubstituted propargylic alcohols (commercially avalaible) according to a previously described procedure.[284]

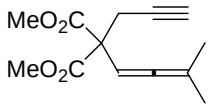
To a suspension of NaH (60% in mineral oil, 1.2 equiv, 6.3 mmol), in anhydrous THF (15 mL) under Ar and cooled at 0 ºC, was added a solution of dimethyl malonate derivative (1 equiv, 5.3 mmol) in anhydrous THF (5 mL), and the mixture was stirred for 15 min at r.t. Then, a solution of bromoallene (1.8 equiv, 9.5 mmol) in anhydrous

[284] Löfstedt, J.; Franzén, J.; Bäckvall, J-E. *J. Org. Chem. Soc.* **2001**, *66*, 8015-8025.

THF (5 mL) was added and the resulting mixture was refluxed for indicated time. Most of the solvent was removed under vacuum and, then, water and Et_2O were added into the resulting mixture. The aqueous layer was separated and extracted with Et_2O (5 x 30 mL). The combined organic phases were dried over anhydrous Mg_2SO_4 and filtered through anhydrous Na_2SO_4. The solvent was removed under vacuum and the residue was purified by column chromatography (hexane:EtOAc).

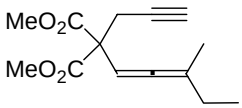
5.1.1 Experimental data of 1,5-allenynes

Dimethyl 2-(3-methylbuta-1,2-dienyl)-2-(prop-2-ynyl)malonate (60a)



Starting from dimethyl propargylmalonate (Fluka) and 1-bromo-3-methylbuta-1,2-diene, and following general procedure for alkylation (19 h), **60a** was obtained in 23% yield as a yellowish oil (hexane/EtOAc, 20:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.56 (sept, J = 2.9 Hz, 1H), 3.75 (s, 6H), 2.88 (d, J = 2.7 Hz, 2H), 1.97 (t, J = 2.7 Hz, 1H), 1.71 (d, J = 2.9 Hz, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 201.9 (C), 169.9 (C), 101.0 (C), 87.8 (CH), 79.7 (C), 70.8 (CH), 57.8 (C), 53.1 (CH_3), 24.5 (CH_2), 20.1 (CH_3). HRMS-ESI+ $[MH]^+$ Calc. for $C_{13}H_{17}O_4$: 237.1121; found: 237.1123.

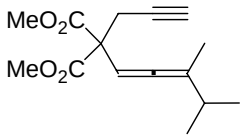
Dimethyl 2-(3-methylpenta-1,2-dienyl)-2-(prop-2-ynyl)malonate (60b)



Starting from dimethyl propargylmalonate (Fluka) and 1-bromo-3-methylpenta-1,2-diene, and following general procedure for alkylation (22 h), **60b** was obtained in 27% yield as a yellowish oil (hexane/EtOAc, 17:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.68 (sext, J = 2.9 Hz, 1H), 3.76 (s, 3H), 3.75 (s, 3H), 2.88 (d, J = 2.6 Hz, 2H), 2.03-1.93 (m, 3H), 1.72 (d, J = 2.9 Hz, 3H), 0.97 (t, J = 7.4 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$,

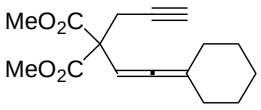
DEPT-135)) δ 201.0 (C), 169.9 (C), 107.4 (C), 89.7 (CH), 79.6 (C), 70.8 (CH), 57.8 (C), 53.1 (CH_3), 53.1 (CH_3), 27.0 (CH_2), 24.7 (CH_2), 18.6 (CH_3), 12.1 (CH_3). HRMS-ESI+ $[MH]^+$ Calc. for $C_{14}H_{19}O_4$: 251.1277; found: 251.1270. Anal. Calc. for $C_{14}H_{18}O_4$: C, 67.18; H, 7.25; found: C, 66.89; H, 7.22.

Dimethyl 2-(3,4-dimethylpenta-1,2-dienyl)-2-(prop-2-ynyl)malonate (60c)



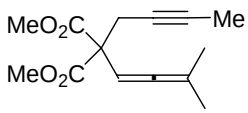
Starting from dimethyl propargylmalonate (Fluka) and 1-bromo-3,4-dimethylpenta-1,2-diene, and following general procedure for alkylation (21 h), **60c** was obtained in 29% yield as a yellowish oil (hexane/EtOAc, 20:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.69 (quint, J = 2.7 Hz, 1H), 3.76 (s, 3H), 3.74 (s, 3H), 2.88 (d, J = 2.7 Hz, 2H), 2.14 (septd, J = 6.8 Hz, J = 2.71 Hz, 1H), 1.97 (t, J = 2.7 Hz, 1H), 1.72 (d, J = 2.7 Hz, 3H), 1.01 (d, J = 6.8 Hz, 3H), 0.99 (d, J = 6.8 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135)) δ 200.3 (C), 169.9 (C), 169.8 (C), 111.6 (C), 89.9 (CH), 79.6 (C), 70.9 (CH), 57.8 (C), 53.0 (CH_3), 53.0 (CH_3), 32.2 (CH), 24.7 (CH_2), 21.4 (CH_3), 21.2 (CH_3), 16.8 (CH_3). TOF MS-EI+ Calc. for $C_{15}H_{20}O_4$: 264.1362; found: 264.1371.

Dimethyl 2-(2-cyclohexylidenevinyl)-2-(prop-2-ynyl)malonate (60d)



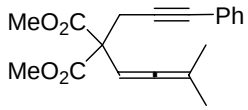
Starting from dimethyl propargylmalonate (Fluka) and (2-bromovinylidene)cyclohexane, and following general procedure for alkylation (23 h), **60d** was obtained in 13% yield as a yellowish oil (hexane/EtOAc, 15:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.57 (quint, J = 2.1 Hz, 1H), 3.75 (s, 6H), 2.89 (d, J = 2.6 Hz, 2H), 2.22-2.03 (m, 4H), 1.96 (t, J = 2.6 Hz, 1H), 1.70-1.42 (m, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135)) δ 198.4 (C), 169.9 (C), 108.1 (C), 87.5 (CH), 79.6 (C), 70.8 (CH), 57.8 (C), 53.1 (CH_3), 31.0 (CH_2), 27.5 (CH_2), 26.1 (CH_2), 24.5 (CH_2). HRMS-ESI+ $[M+Na]^+$ Calc. for $C_{16}H_{20}O_4Na$: 299.1253; found: 299.1247.

Dimethyl 2-(but-2-ynyl)-2-(3-methylbuta-1,2-dienyl)malonate (60e)



Starting from dimethyl 2-(but-2-ynyl)malonate[272] and 1-bromo-3-methylbuta-1,2-diene, and following general procedure for alkylation (17 h), **60e** was obtained in 28% yield as a yellowish oil (hexane/EtOAc, 20:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.54 (sept, J = 2.9 Hz, 1H), 3.74 (s, 6H), 2.81(q, J = 2.5 Hz, 2H), 1.73 (t, J = 2.5 Hz, 3H), 1.71 (d, J = 2.9 Hz, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 201.8 (C), 170.2 (C), 100.8 (C), 88.1 (CH), 78.3 (C), 74.1 (C), 58.2 (C), 53.0 (CH_3), 25.0 (CH_2), 20.2 (CH_3), 3.7 (CH_3). HRMS-ESI+ $[M+Na]^+$ Calc. for $C_{14}H_{18}O_4Na$: 273.1097; found: 273.1090.

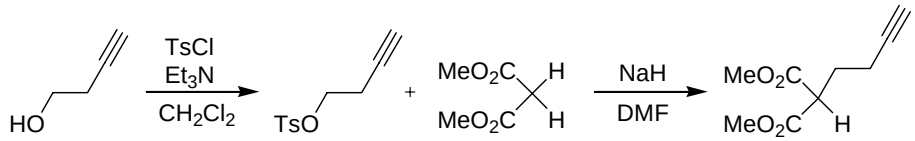
Dimethyl 2-(3-methylbuta-1,2-dienyl)-2-(3-phenylprop-2-ynyl)malonate (60f)



Starting from dimethyl 2-(3-phenylprop-2-ynyl)malonate[261] and 1-bromo-3-methylbuta-1,2-diene, and following general procedure for alkylation (20 h), **60f** was obtained in 28% yield as a yellowish oil (toluene/Et_2O, 40:1). A further column chromatography, using toluene as eluent, was necessary to achieve the complete purification of the product. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.38-7.30 (m, 2H), 7.29-7.22 (m, 3H), 5.61 (sept, J = 2.9 Hz, 1H), 3.78 (s, 6H), 3.10 (s, 2H), 1.73 (d, J = 2.9 Hz, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 201.8 (C), 170.1 (C), 131.7 (CH), 128.3 (CH), 128.0 (CH), 123.6 (C), 101.1 (C), 88.1 (CH), 85.2 (C), 83.0 (C), 58.1 (C), 53.1 (CH_3), 25.5 (CH_2), 20.3 (CH_3). HRMS-ESI+ $[MH]^+$ Calc. for $C_{19}H_{21}O_4$: 313.1434; found: 313.1440.

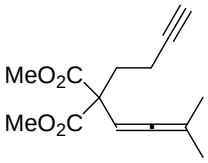
[261] Schiller, R.; Pour, M.; Fakova, H.; Kunes, J.; Cisarova, I. *J. Org. Chem.* **2004**, *69*, 6761-6765.
[272] Zhang, Q.; Xu, W.; Lu, X. *J. Org. Chem.* **2005**, *70*, 1505-1507.

5.1.2 Experimental data of 1,6-allenynes



But-3-ynyl 4-methylbenzenesulfonate was preparated under standar conditions, using *p*-toluenesulfonyl chloride (1.1 equiv), triethylamine (2.1 equiv) and dichloromethane as solvent.[285] Then, to a dry flask containing NaH (60% in mineral oil, 0.491 g, 12.3 mmol) and anhydrous DMF (15 ml) was slowly added a solution of dimethylmalonate (4.42 g, 33.44 mmol) in anhydrous DMF (2.5 ml) at 0 ºC. The solution was stirred for 15 min at r.t. After this, a solution of but-3-ynyl 4-methylbenzenesulfonate (2.5 g, 11.15 mmol) in anhydrous DMF (2.5 ml) was added and the resulting mixture was stirred at 90 ºC for 21 h. Afterwards, the mixture was diluted with water and Et_2O. The aqueous phase was extracted with Et_2O (5 x 15 ml), and the combined organic layers were successively washed with a 10% aqueous solution of HCl (3 x 10 ml) and water (5 x 10 ml). The organic phase was dried over Mg_2SO_4, filtered over anhydrous Na_2SO_4 and the solvent was removed in vacuo. The crude was purified by column chromatography (hexane:EtOAc, 9:1), which gave 1.073 g (52% yield) of dimethyl 2-(but-3-ynyl)malonate.

Dimethyl 2-(but-3-ynyl)-2-(3-methylbuta-1,2-dienyl)malonate (63a)

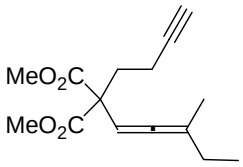


Starting from dimethyl 2-(but-3-ynyl)malonate and 1-bromo-3-methylbuta-1,2-diene, and following general procedure for alkylation (22 h), **63a** was obtained in 41% yield as a yellowish oil (hexane/EtOAc, 20:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.46 (sept, J = 2.9 Hz, 1H), 3.70 (s, 6H), 2.25-2.11 (m, 4H), 1.92 (t, J = 2.5 Hz, 1H), 1.68 (d, J = 2.9 Hz, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 201.7 (C), 170.6 (C), 100.5 (C), 88.0 (CH), 83.6 (C), 68.6 (CH), 57.5 (C), 52.8 (CH_3), 33.3 (CH_2), 20.0 (CH_3), 14.2 (CH_2).

[285] Naumann, C.; Patrick, B. O.; Sherman, J. C. *Tetrahedron Lett.* **2002**, *43*, 787-790.

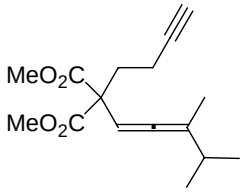
HRMS-ESI+ $[MH]^+$ Calc. for $C_{14}H_{19}O_4$: 251.1277; found: 251.1283. Anal. Calc. for $C_{14}H_{18}O_4$: C, 67.18; H, 7.25; found: C, 67.21; H, 7.38.

Dimethyl 2-(but-3-ynyl)-2-(3-methylpenta-1,2-dienyl)malonate (63b)



Starting from dimethyl 2-(but-3-ynyl)malonate and 1-bromo-3-methylpenta-1,2-diene, and following general procedure for alkylation (24 h), **63b** was obtained in 26% yield as a white solid (hexane/EtOAc, 16:1), mp 41-43 ºC. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.58 (sext, J = 2.8 Hz, 1H), 3.71 (s, 3H), 3.70 (s, 3H), 2.27-2.11 (m, 4H), 2.01-1.90 (m, 3H), 1.69 (d, J = 2.8 Hz, 3H), 0.95 (t, J = 7.4 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 200.8 (C), 170.6 (C), 106.9 (C), 89.9 (CH), 83.6 (C), 68.6 (CH), 57.6 (C), 52.8 (CH_3), 33.4 (CH_2), 27.0 (CH_2), 18.6 (CH_3), 14.3 (CH_2), 12.0 (CH_3). HRMS-ESI+ $[M+Na]^+$ Calc. for $C_{15}H_{20}O_4Na$: 287.1253; found: 287.1273. Anal. Calc. for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63; found: C, 67.88; H, 7.56.

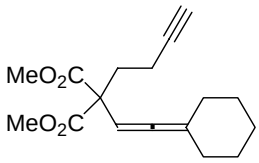
Dimethyl 2-(but-3-ynyl)-2-(3,4-dimethylpenta-1,2-dienyl)malonate (63c)



Starting from dimethyl 2-(but-3-ynyl)malonate and 1-bromo-3,4-dimethylpenta-1,2-diene, and following general procedure for alkylation (22 h), **63c** was obtained in 16% yield as a colorless oil (hexane/EtOAc, 15:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.59 (quint, J = 2.8 Hz, 1H), 3.72 (s, 3H), 3.71 (s, 3H), 2.30-2.05 (m, 5H), 1.95-1.91 (m, 1H), 1.70 (d, J = 2.8 Hz, 3H), 1.00 (d, J = 2.4 Hz, 3H), 0.98 (d, J = 2.4 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 200.2 (C), 170.6 (C), 111.0 (C), 89.9 (CH), 83.4 (C), 68.5 (CH), 57.4 (C), 52.6 (CH_3), 33.5 (CH_2), 32.3 (CH), 21.6 (CH_3), 21.3 (CH_3), 16.9

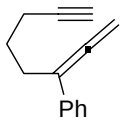
(CH_3), 14.3 (CH_2). HRMS-ESI+ $[M]^+$ Calc. for $C_{16}H_{22}O_4$: 278.1518; found: 278.1523. Anal. Calc. for $C_{16}H_{22}O_4$: C, 69.04; H, 7.97; found: C, 68.84; H, 8.11.

Dimethyl 2-(but-3-ynyl)-2-(2-cyclohexylidenevinyl)malonate (63d)



Starting from dimethyl 2-(but-3-ynyl)malonate and (2-bromovinylidene)cyclohexane, and following general procedure for alkylation (20 h), **63d** was obtained in 12% yield as a yellowish oil (hexane/EtOAc, 16:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.47 (quint, J = 2 Hz, 1H), 3.72 (s, 6H), 2.29-2.21 (m, 2H), 2.20-2.02 (m, 6H), 1.93 (t, J = 2.5 Hz, 1H), 1.70-1.41 (m, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 198.3 (C), 170.7 (C), 107.7 (C), 87.7 (CH), 83.6 (C), 68.7 (CH), 57.6 (C), 52.8 (CH_3), 33.2 (CH_2), 31.1 (CH_2), 27.4 (CH_2), 26.1 (CH_2), 14.2 (CH_2). HRMS-ESI+ $[M]^+$ Calc. for $C_{17}H_{22}O_4$: 290.1518; found: 290.1516. Anal. Calc. for $C_{17}H_{22}O_4$: C, 70.32; H, 7.64; found: C, 70.40; H, 7.83.

Octa-1,2-dien-7-yn-3-ylbenzene (63e)



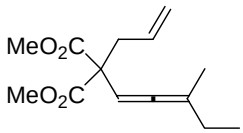
This compound was prepared according to previosly described procedure.[286] ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.45-7.39 (m, 2H), 7.36-7.29(m, 2H), 7.24-7.17 (m, 1H), 5.10 (t, J = 3.3 Hz, 2H), 2.60-2.51 (m, 2H), 2.31 (dt, J = 7.1 Hz, J = 2.7 Hz, 2H), 1.98 (t, J = 2.7 Hz, 1H), 1.87-1.76 (m, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 208.6 (C), 136.3 (C), 128.6 (CH), 126.9 (CH), 126.1 (CH), 104.4 (C), 84.4 (C), 78.7 (CH_2), 68.7 (CH), 28.6 (CH_2), 26.9 (CH_2), 18.3 (CH_2). HRMS-EI+ $[M]^+$ Calc. for $C_{14}H_{14}$: 182.1096; found: 182.1089.

[286] Lee, K.; Seomoon, D.; Lee, P. H. Angew. Chem. Int. Ed. **2002**, 41, 3901-3903.

5.1.3 Experimental data of 1,5-enallenes

Enallenes **66a** and **70** have been previously described in the literature and was prepared accoding to those procedures.[243d]

Dimethyl 2-allyl-2-(3-methylpenta-1,2-dienyl)malonate (66b)



Starting from dimethyl allylmalonate (Aldrich) and 1-bromo-3-methylpenta-1,2-diene, and following general procedure for alkylation (14 h), **66b** was obtained in 10% yield as a yellowish oil (hexane/EtOAc, 30:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.69 (ddt, J = 17.3 Hz, J = 9.6 Hz, J = 7.1 Hz, 1H), 5.58 (sext, J = 2.9 Hz, 1H), 5.05 (d, J = 17.3 Hz, 1H), 5.03 (d, J = 9.6 Hz, 1H), 3.69 (s, 3H), 3.68 (s, 3H), 2.71 (d, J = 7.1 Hz, 2H), 1.94 (dq, J = 7.4 Hz, J = 2.9 Hz, 2H), 1.67 (d, J = 2.9 Hz, 3H), 0.94 (t, J = 7.4 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135)) δ 201.0 (C), 170.8 (C), 133.1 (CH), 118.6 (CH_2), 106.5 (C), 90.3 (CH), 58.6 (C), 52.7 (CH_3), 39.3 (CH_2), 27.0 (CH_2), 18.7 (CH_3), 12.1 (CH_3). HRMS-ESI+ $[MH]^+$ Calc. for $C_{14}H_{21}O_4$: 253.1434; found: 253.1442.

5.2 General optimized procedure for the synthesis of allyl- and alkylboronates from allenynes and enallenes

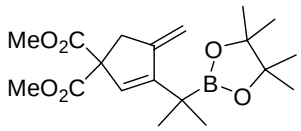
The corresponding allenyne or enallene (*ca.* 50 mg), bis(pinacolato)diboron (1.2 equiv), and $Pd(OAc)_2$ (5 mol %) were sequentially added to a 5 mL flask. After purging with Ar, anhydrous toluene (1 mL) and anhydrous MeOH (1 equiv) were added. Then, the mixture was stirred during the corresponding time at the temperature indicated below for each compound. After cooling the mixture to room temperature, the solvent was evaporated and the column chromatography (Hexane:EtOAc) afforded the product. Partial decomposition of the products was detected when using long retention times, probably due to the hydrolysis of the pinacolboronate moiety.

[243] Franzén, J.; Bäckvall, J. *J. Am. Chem. Soc.* **2003**, *125*, 6056-6057.

5.2.1 Experimental data of allyl- and alkylboronates

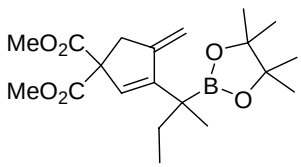
5.2.1.1 Experimental data of allylboronates from 1,5-allenynes

Dimethyl 4-methylene-3-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propan-2-yl)cyclopent-2-ene-1,1-dicarboxylate (61a)



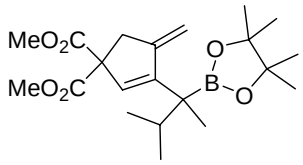
Following general borylative cyclization procedure (using 10 mol% of the catalyst), **61a** was obtained after 4 h (50 ºC) in 62% isolated yield (80% calculated by NMR) as a yellowish oil (hexane/EtOAc 10:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.88 (broad s, 1H), 4.99-4.96 (m, 1H), 4.94-4.90 (m, 1H), 3.72 (s, 6H), 3.14 (t, J = 1.9 Hz, 2H), 1.19 (broad s, 18H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 171.5 (C), 155.3 (C), 149.6 (C), 128.4 (CH), 104.9 (CH_2), 83.6 (C), 63.0 (C), 53.0 (CH_3), 39.2 (CH_2), 24.7 (CH_3), 24.4 (CH_3). HRMS-ESI+ $[MH]^+$ Calc. for $C_{19}H_{30}BO_6$: 365.2129; found: 365.2142.

Dimethyl 4-methylene-3-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butan-2-yl)cyclopent-2-ene-1,1-dicarboxylate (61b)



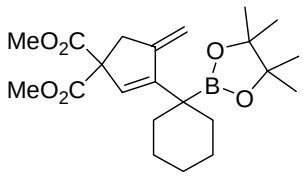
Following general borylative cyclization procedure, **61b** was obtained after 4 h (50 ºC) in 60% yield as a colorless oil (hexane/EtOAc 15:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.89 (broad s, 1H), 5.08-5.05 (m, 1H), 4.94-4.90 (m, 1H), 3.73 (s, 3H), 3.71 (s, 3H), 3.22-3.06 (m, 2H), 1.82-1.59 (m, 2H), 1.20 (broad s, 12H), 1.16 (s, 3H), 0.76 (t, J = 7.4 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 171.6 (C), 171.4 (C), 153.5 (C), 149.6 (C), 130.0 (CH), 104.9 (CH_2), 83.6 (C), 63.0 (C), 52.9 (CH_3), 39.3 (CH_2), 28.8 (CH_2), 24.9 (CH_3), 20.2 (CH_3), 8.8 (CH_3). HRMS-ESI+ $[MH]^+$ Calc. for $C_{20}H_{32}BO_6$: 379.2286; found: 379.2287.

Dimethyl 3-(3-methyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butan-2-yl)-4-methylenecyclopent-2-ene-1,1-dicarboxylate (61c)



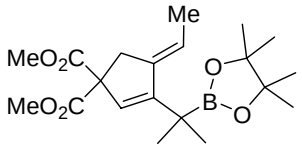
Following general borylative cyclization procedure, **61c** was obtained after 14 h (-20 ºC) in 40% yield as a yellowish oil (hexane/EtOAc 15:1). When the reaction was carried out at r.t. or 50 ºC was observed an unidentified byproduct that could not be separated from **60c**. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.91 (broad s, 1H), 5.33-5.29 (m, 1H), 4.96-4.92 (m, 1H), 3.72 (broad s, 3H), 3.71 (broad s, 3H), 3.22-3.01 (m, 2H), 2.44 (sept, J = 6.8 Hz, 1H), 1.20 (s, 6H), 1.18 (s, 6H), 1.08 (s, 3H), 0.97 (d, J = 6.8 Hz, 3H), 0.65 (d, J = 6.8 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 171.7 (C), 171.3 (C), 153.3 (C), 149.2 (C), 130.8 (CH), 105.9 (CH_2), 83.5 (C), 62.8 (C), 52.9 (CH_3), 52.8 (CH_3), 39.9 (CH_2), 30.0 (CH), 25.0 (CH_3), 24.6 (CH_3), 20.2 (CH_3), 16.7 (CH_3), 14.6 (CH_3). HRMS-ESI+ $[M+Na]^+$ Calc. for $C_{21}H_{33}BO_6Na$: 414.2298; found: 414.2294.

Dimethyl 4-methylene-3-(1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclohexyl)cyclopent-2-ene-1,1-dicarboxylate (61d)



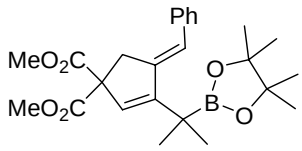
Following general borylative cyclization procedure, **61d** was obtained after 4 h (50 ºC) in 73% yield as a white solid (hexane/EtOAc 14:1), mp 84-87 ºC. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.90 (broad s, 1H), 5.32-5.28 (m, 1H), 4.97-4.92 (m, 1H), 3.71 (s, 6H), 3.09 (t, J = 1.9 Hz, 2H), 2.27-2.14 (m, 2H), 1.75-1.57 (m, 4H), 1.50-1.27 (m, 4H), 1.20 (s, 12H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 171.5 (C), 154.1 (C), 149.0 (C), 129.2 (CH), 106.0 (CH_2), 83.6 (C), 62.8 (C), 52.9 (CH_3), 39.8 (CH_2), 34.0 (CH_2), 26.7 (CH_2), 25.0 (CH_2), 24.9 (CH_3). HRMS-ESI+ $[MH]^+$ Calc. for $C_{22}H_{34}BO_6$: 405.2442; found: 405.2456. Anal. Calc. for $C_{22}H_{33}BO_6$: C, 65.36; H, 8.23; found: C, 65.09; H, 8.13.

(*E*)-Dimethyl 4-ethylidene-3-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propan-2-yl)cyclopent-2-ene-1,1-dicarboxylate (61e)



Following general borylative cyclization procedure, **61e** was obtained after 51 h (rt to 50 ºC) in 36% yield as a yellowish oil (hexane/EtOAc 14:1). After 48 h, additional $Pd(OAc)_2$ (5 mol%) and B_2pin_2 (1 equiv) were added and heated at 50 ºC. Partial decomposition of the boronate was detected. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.8 (s, 1H), 5.52-5.46 (m, 1H), 3.78 (s, 6H), 3.14 (broad s, 2H), 1.73-1.71 (m, J = 6.91 Hz, 3H), 1.24 (s, 12H), 1.23 (s, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 171.9 (C), 155.5 (C), 142.5 (C), 125.3 (CH), 115.5 (CH), 83.5 (C), 63.1 (C), 52.9 (CH_3), 36.1 (CH_2), 24.7 (CH_3), 24.6 (CH_3), 14.7 (CH_3). HRMS-ESI+ $[MH]^+$ Calc. for $C_{20}H_{32}BO_6$: 379.2286; found: 379.2280.

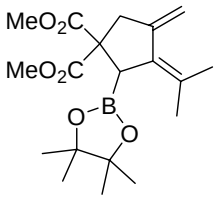
(*E*)-Dimethyl 4-benzylidene-3-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propan-2-yl)cyclopent-2-ene-1,1-dicarboxylate (61f)



Following general borylative cyclization procedure, **61f** was obtained after 1.5 h (rt) in 37% yield as a crystalline white solid (hexane/EtOAc 12:1 to 10:1), mp 122-124 ºC. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.41-7.30 (m, 4H), 7.23-7.16 (m, 1H), 6.42 (t, J = 2.2 Hz, 1H), 5.96 (s, 1H), 3.74 (s, 6H), 3.48 (d, J = 2.2 Hz, 2H), 1.28 (s, 6H), 1.21 (s, 12H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 171.5 (C), 156.9 (C), 143.5 (C), 137.9 (C), 128.6 (CH), 128.6 (CH), 127.5 (CH), 126.5 (CH), 121.1 (CH), 83.7 (C), 64.1 (C), 53.1 (CH_3), 38.5 (CH_2), 24.8 (CH_3). HRMS-ESI+ $[M+Na]^+$ Calc. for $C_{25}H_{33}BO_6Na$: 463.2262; found: 463.2270.

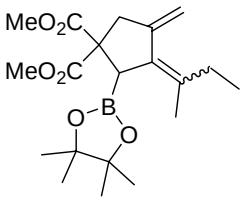
Endocyclic boronates **62a**, **62b**, **62d** and **62f** could not be isolated as pure compounds as a result of their instability and fast decomposition in solution, which also precluded their complete characterization.

Dimethyl 4-methylene-3-(propan-2-ylidene)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (62a)



Following general borylative cyclization procedure (using 10 mol% of the catalyst), **62a** was obtained after 4 h (50 ºC) in 1% isolated yield (2% calculated by NMR) as a yellowish oil (hexane/EtOAc 10:1). Partial decomposition of the boronate was detected. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.10 (broad s, 1H), 5.10 (broad s, 1H), 3.70 (s, 3H), 3.67 (s, 3H), 3.22 (dt, J = 15.5, 2.7 Hz, 1H), 3.12 (broad s, 1H), 3.05-2.95 (m, 1H), 1.91 (s, 3H), 1.83 (s, 1H), 1.18 (s, 6H), 1.16 (s, 6H). HRMS-ESI+ $[MH]^+$ Calc. for $C_{19}H_{30}BO_6$: 365.2129; found: 365.2138.

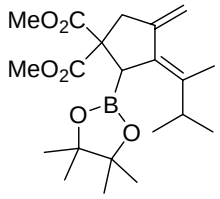
(*Z*,*E*)-Dimethyl 3-(butan-2-ylidene)-4-methylene-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (62b)



Following general borylative cyclization procedure, **62b** was obtained after 4 h (50 ºC) in 3% yield (7% calculated by NMR) as a colorless oil (hexane/EtOAc 15:1). Partial decomposition of the boronate was detected. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.08 (broad s, 2H), 3.70 (s, 3H), 3.66 (s, 3H), 3.21 (dt, J = 15.8, 2.7 Hz, 1H), 3.13 (broad s, 1H), 3.09-3.00 (m, 1H), 2.38-2.23 (m, 1H), 2.05-1.90 (m, 1H), 1.88 (s, 3H), 1.18 (s, 6H),

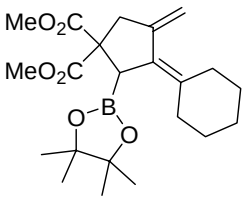
1.16 (s, 6H), 0.98 (t, J = 7.5 Hz, 3H). HRMS-ESI+ $[MH]^+$ Calc. for $C_{20}H_{32}BO_6$: 379.2286; found: 379.2289.

(*E*)-Dimethyl 3-(3-methylbutan-2-ylidene)-4-methylene-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (62c)



Following general borylative cyclization procedure, **62c** was obtained after 14 h (-20 ºC) in 13% yield (20% calculated by NMR) as a yellowish oil (hexane/EtOAc 15:1). Double bond configuration determined by NOE experiments. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.08 (broad s, 2H), 3.70 (s, 3H), 3.65 (s, 3H), 3.21-3.16 (m, 2H), 3.10-3.01 (m, 1H), 2.83 (sept, J = 6.8 Hz, 1H), 1.75 (s, 3H), 1.19 (s, 6H), 1.16 (s, 6H), 0.98 (d, J = 6.8 Hz, 3H), 0.91 (d, J = 6.8 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.5 (C), 172.0 (C), 146.0 (C), 138.9 (C), 130.1 (C), 109.6 (CH_2), 83.4 (C), 59.8 (C), 52.8 (CH_3), 52.7 (CH_3), 41.5 (CH_2), 33.3 (CH), 25.0 (CH_3), 24.6 (CH_3), 20.2 (CH_3), 20.1 (CH_3), 14.6 (CH_3). HRMS-ESI+ $[MH]^+$ Calc. for $C_{21}H_{34}BO_6$: 414.2298; found: 414.2294.

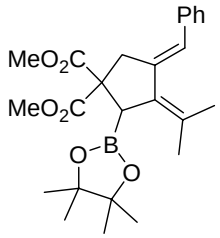
Dimethyl 3-cyclohexylidene-4-methylene-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (62d)



Following general borylative cyclization procedure, **62d** was obtained after 4 h (50 ºC) in 7% yield as a colorless oil (hexane/EtOAc 14:1). Partial decomposition of the boronate was detected. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.12 (broad s, 1H), 5.04 (broad s,

1H), 3.70 (s, 3H), 3.67 (s, 3H), 3.21-3.12 (m, 2H), 3.05-2.96 (m, 1H), 2.57-2.38 (m, 2H), 2.28-2.16 (m, 2H), 1.62-1.46 (m, 6H), 1.18 (broad s, 6H), 1.17 (broad s, 6H).

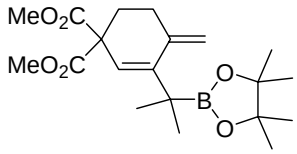
(*E*)-Dimethyl 4-benzylidene-3-(propan-2-ylidene)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (62f)



Following general borylative cyclization procedure, **62f** was obtained after 1.5 h (rt) in 5% yield as a colorless oil (hexane/EtOAc 12:1 to 10:1). Partial decomposition of the boronate was detected. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.38-7.28 (m, 4H), 7.23-7.13 (m, 1H), 6.59 (broad s, 1H), 3.71 (s, 3H), 3.62 (s, 3H), 3.46-3.35 (m, 1H), 3.33-3.23 (m, 1H), 3.14 (broad s, 1H), 2.04 (s, 3H), 1.88 (s, 3H), 1.17 (broad s, 6H), 1.16 (broad s, 6H). HRMS-ESI+ $[M+Na]^+$ Calc. for $C_{25}H_{33}BO_6Na$: 463.2262; found: 463.2242.

5.2.1.2 Experimental data of allylboronates from 1,6-allenynes

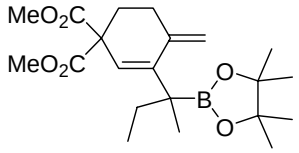
Dimethyl 4-methylene-3-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propan-2-yl)cyclohex-2-ene-1,1-dicarboxylate (64a)



Following general borylative cyclization procedure, **64a** was obtained after 22 h (rt) in 45% yield as a white solid (hexane/EtOAc 10:1), mp 69-72 ºC. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.79 (s, 1H), 5.0 (broad s, 1H), 4.93-4.89 (m, 1H), 3.72 (s, 6H), 2.44-2.36 (m, 2H), 2.20-2.13 (m, 2H), 1.18 (broad s, 12H), 1.18 (broad s, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 171.6 (C), 146.5 (C), 141.3 (C), 119.9 (CH), 111.2 (CH_2), 83.3

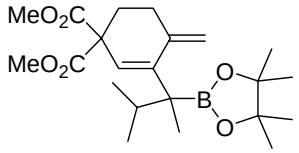
(C), 56.0 (C), 52.9 (CH_3), 30.7 (CH_2), 29.3 (CH_2), 25.5 (CH_3), 24.7 (CH_3). HRMS-ESI+ $[MH]^+$ Calc. for $C_{20}H_{32}BO_6$: 379.2286; found: 379.2289.

Dimethyl 4-methylene-3-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butan-2-yl)cyclohex-2-ene-1,1-dicarboxylate (64b)



Following general borylative cyclization procedure, **64b** was obtained after 4 h (50 ºC) in 43% yield as a white solid (hexane/EtOAc 15:1 to 10:1), mp 53-56 ºC. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.73 (broad s, 1H), 5.03 (broad s, 1H), 4.91-4.88 (m, 1H), 3.74 (s, 3H), 3.71 (s, 3H), 2.43-2.34 (m, 2H), 2.22-2.13 (m, 2H), 1.90-1.73 (m, 1H), 1.64-1.50 (m, 1H), 1.20 (broad s, 6H), 1.19 (broad s, 6H), 1.33 (s, 3H), 0.70 (t, J = 7.5 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 171.7 (C), 171.8 (C), 144.0 (C), 141.4 (C), 121.8 (CH), 111.1 (CH_2), 83.2 (C), 56.2 (C), 52.9 (CH_3), 52.8 (CH_3), 30.9 (CH_2), 29.4 (CH_2), 29.1 (CH_2), 24.8 (CH_3), 24.8 (CH_3), 21.0 (CH_3), 8.3 (CH_3). HRMS-ESI+ $[MH]^+$ Calc. for $C_{21}H_{34}BO_6$: 393.2442; found: 393.2443.

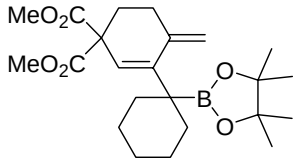
Dimethyl 3-(3-methyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butan-2-yl)-4-methylenecyclohex-2-ene-1,1-dicarboxylate (64c)



Following general borylative cyclization procedure, **64c** was obtained after 24 h (rt) in 12% yield as a yellowish oil (hexane/EtOAc 15:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.74 (s, 1H), 5.27 (s, 1H), 4.90 (s, 1H), 3.74 (s, 3H), 3.70 (s, 3H), 2.40-2.33 (m, 3H), 2.21-2.13 (m, 2H), 1.20 (s, 6H), 1.17 (s, 6H), 1.05 (s, 3H), 1.00 (d, J = 6.8 Hz, 3H), 0.62 (d, J = 6.8 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 171.8 (C), 171.6 (C), 145.0 (C), 141.6 (C), 121.8 (CH), 111.7 (CH_2), 83.1 (C), 56.4 (C), 52.9 (CH_3), 52.8 (CH_3),

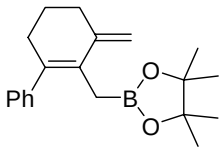
31.5 (CH_2), 30.8 (CH), 29.6 (CH_2), 25.0 (CH_3), 24.6 (CH_3), 20.2 (CH_3), 17.3 (CH_3), 15.9 (CH_3). HRMS-ESI+ $[M+Na]^+$ Calc. for $C_{22}H_{35}BO_6Na$: 429.2418; found: 429.2401.

Dimethyl 4-methylene-3-(1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclohexyl)cyclohex-2-ene-1,1-dicarboxylate (64d)



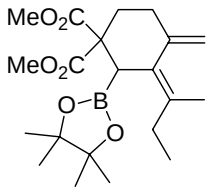
Following general borylative cyclization procedure, **64d** was obtained after 1 h (rt) in 57% yield as a white solid (hexane/EtOAc 10:1), mp 57-60 ºC. Partial decomposition of the boronate was detected. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.80 (s, 1H), 5.30 (s, 1H), 4.90 (s, 1H), 3.73 (s, 6H), 2.38-2.30 (m, 2H), 2.21-2.14 (m, 2H), 2.13-2.04 (m, 2H), 1.77-1.31 (m, 8H), 1.20 (s, 12H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 171.7 (C), 146.0 (C), 141.1 (C), 120.8 (CH), 112.2 (CH_2), 83.2 (C), 56.3 (C), 52.9 (CH_3), 34.7 (CH_2), 31.7 (CH_2), 29.7 (CH_2), 27.0 (CH_2), 24.9 (CH_3), 24.5 (CH_2). HRMS-ESI+ $[M+Na]^+$ Calc. for $C_{23}H_{35}BO_6Na$: 441.2418; found: 441.2419.

4,4,5,5-Tetramethyl-2-((6-methylene-2-phenylcyclohex-1-enyl)methyl)-1,3,2-dioxaborolane (64e)



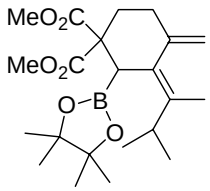
Following general borylative cyclization procedure, **64e** was obtained after 24 h (50 ºC) in 12% yield as a yellowish oil (hexane/EtOAc 30:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.35-7.26 (m, 3H), 7.25-7.17 (m, 2H), 4.91 (broad s, 1H), 4.80 (broad s, 1H), 2.50-2.40 (m, 4H), 1.80 (quint, J = 6.3 Hz, 2H), 1.36-1.26 (m, 2H), 1.21 (broad s, 12H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 145.9 (C), 144.7 (C), 138.0 (C), 129.9 (C), 128.5 (CH), 128.1 (CH), 126.4 (CH), 108.3 (CH_2), 83.2 (C), 33.7 (CH_2), 33.1 (CH_2), 29.9 (CH_2), 24.8 (CH_3), 23.9 (CH_2). HRMS-EI+ $[M]^+$ Calc. for $C_{20}H_{27}BO_6$: 310.2104; found: 310.2092.

(*E*)-Dimethyl 3-(butan-2-ylidene)-4-methylene-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclohexane-1,1-dicarboxylate (65b)



Following general borylative cyclization procedure, **65b** was obtained after 3 h (rt) in 4% yield as a white solid (hexane/EtOAc 20:1). Double bond configuration determined by NOE experiments. The stereoisomer of this compound was also observed, but it could not be isolated due to the low yield and partial decomposition. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.96-4.94 (m, 1H), 4.53-4.51 (m, 1H), 3.68 (s, 3H), 3.65 (s, 3H), 3.38 (broad s, 1H), 2.42-2.34 (m, 2H), 2.34-2.24 (m, 3H), 2.07-1.99 (m, 1H), 1.75(s, 3H), 1.18 (s, 6H), 1.13 (s, 6H), 1.01 (t, J = 7.6 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.8 (C), 171.9 (C), 146.0 (C), 133.4 (C), 129.0 (C), 112.3 (CH_2), 83.6 (C), 57.5 (C), 52.8 (CH_3), 52.4 (CH_3), 33.2 (CH_2), 29.9 (CH_2), 27.1 (CH_2), 25.0 (CH_3), 24.5 (CH_3), 19.9 (CH_3), 12.9 (CH_3). HRMS-ESI+ $[M+Na]^+$ Calc. for $C_{21}H_{33}BO_6Na$: 415.2262; found: 415.2257.

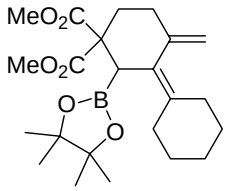
(*E*)-Dimethyl 3-(3-methylbutan-2-ylidene)-4-methylene-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclohexane-1,1-dicarboxylate (65c)



Following general borylative cyclization procedure, **65c** was obtained after 24 h (rt) in 35% yield (41% calculated by NMR) as a white solid (hexane/EtOAc 15:1). Double bond configuration determined by NOE experiments and X-ray diffraction. The stereoisomer of this compound was observed by NMR in 6% yield. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.98-4.94 (m, 1H), 4.53-4.49 (m, 1H), 3.67 (s, 3H), 3.64 (s, 3H), 3.48 (broad s, 1H), 3.10 (sept, J = 6.8 Hz, 1H), 2.45-2.15 (m, 4H), 1.64 (s, 3H), 1.17 (s, 6H),

1.12 (s, 6H), 0.99 (d, J = 6.8 Hz, 3H), 0.93 (d, J = 6.8 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.8 (C), 171.9 (C), 146.3 (C), 136.8 (C), 128.2 (C), 112.7 (CH_2), 83.1 (C), 57.4 (C), 52.8 (CH_3), 52.5 (CH_3), 33.2 (CH_2), 30.1 (CH_2), 29.5 (CH), 25.1 (CH_3), 24.4 (CH_3), 21.2 (CH_3), 20.5 (CH_3), 13.9 (CH_3). HRMS-ESI+ $[M+Na]^+$ Calc. for $C_{22}H_{35}BO_6Na$: 429.2418; found: 429.2412. Anal. Calc. for $C_{22}H_{35}BO_6$: C, 65.03; H, 8.68; found: C, 64.92; H, 8.61.

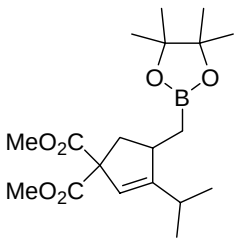
Dimethyl 6-methylene-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,1'-bi(cyclohexylidene)-3,3-dicarboxylate (65d)



Following general borylative cyclization procedure, **65d** was obtained after 1 h (rt) in 40% yield as a yellowish oil (hexane/EtOAc 10:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.89 (broad s, 1H), 4.52-4.48 (m, 1H), 3.68 (s, 3H), 3.66 (s, 3H), 3.45 (broad s, 1H), 2.48-2.24 (m, 5H), 2.23-2.07 (m, 3H), 1.58-1.52 (m, 6H), 1.18 (s, 6H), 1.14 (s, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.7 (C), 171.8 (C), 145.9 (C), 136.3 (C), 126.7 (C), 111.3 (CH_2), 83.1 (C), 57.6 (C), 52.8 (CH_3), 33.4 (CH_2), 32.2 (CH_2), 30.8 (CH_2), 30.1 (CH_2), 29.6 (CH_2), 28.7 (CH_2), 27.3 (CH_2), 25.1 (CH_3), 24.5 (CH_3). HRMS-ESI+ $[MH]^+$ Calc. for $C_{23}H_{36}BO_6$: 419.2599; found: 419.2599.

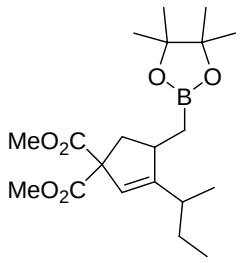
5.2.1.3 Experimental data of alkyl- and allylboronates from 1,5-enallenes

Dimethyl 3-isopropyl-4-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)cyclopent-2-ene-1,1-dicarboxylate (67a)



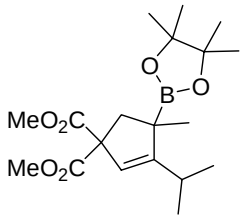
Following general borylative cyclization procedure, **67a** was obtained after 3 h (70 ºC) in 52% yield (calculated by NMR) as a colorless oil (hexane/EtOAc 20:1). Partial decomposition of the boronate was detected. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.36 (broad s, 1H), 3.70 (broad s, 3H), 3.70 (broad s, 3H), 3.06-2.92 (m, 1H), 2.80 (dd, J = 13.4, 7.9 Hz, 1H), 2.30 (sept, J = 6.7 Hz, 1H), 1.95 (dd, J = 13.4, 6.7 Hz, 1H), 1.22 (broad s, 12H), 1.10 (d, J = 6.7 Hz, 3H), 0.96 (d, J = 6.7 Hz, 3H), 1.08-1.00 (m, 1H), 0.68 (dd, J = 15.4, 10.3 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.7 (C), 172.3 (C), 160.6 (C), 118.9 (CH), 83.3 (C), 64.8 (C), 52.7 (CH_3), 52.6 (CH_3), 41.1 (CH), 40.3 (CH_2), 27.2 (CH), 25.1 (CH_3), 24.9 (CH_3), 21.6 (CH_3), 21.0 (CH_3). HRMS-ESI+ $[MH]^+$ Calc. for $C_{19}H_{32}BO_6$: 367.2286; found: 367.2295.

Dimethyl 3-*sec*-butyl-4-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)cyclopent-2-ene-1,1-dicarboxylate (67b)



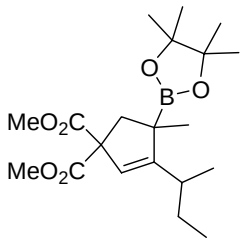
Following general borylative cyclization procedure, **67b** was obtained after 16 h (50 ºC) in 30% yield (calculated by NMR) as a colorless oil (hexane/EtOAc 20:1). Mixture of two diasteroisomers (60:40). Partial decomposition of the boronate was detected. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.39-5.37 (m, 1H), 5.36-5.34 (m, 1H), 3.71 (s, 3H), 3.71 (s, 3H), 3.68 (s, 3H), 3.68 (s, 3H), 3.04-2.88 (m, 2H), 2.79 (dd, J = 13.3, 7.9 Hz, 2H), 2.22 (quint, J = 6.2 Hz, 1H), 2.10-1.99 (m, 1H), 1.95 (dd, J = 13.3, 7.8 Hz, 2H), 1.67-1.27 (m, 2H), 1.23 (broad s, 24H), 1.06 (d, J = 6.8 Hz, 3H), 0.96 (d, J = 6.9 Hz, 3H), 0.89 (t, J = 7.4 Hz, 3H), 0.76 (t, J = 7.4 Hz, 3H), 0.68 (dd, J = 15.5, 10.4 Hz, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.7 (C), 172.6 (C), 172.4 (C), 172.3 (C), 159.6 (C), 159.1 (C), 120.2 (CH), 119.3 (CH), 83.3 (C), 64.9 (C), 64.8 (C), 52.7 (CH_3), 52.7 (CH_3), 41.6 (CH), 41.4 (CH), 40.3 (CH_2), 40.2 (CH_2), 34.5 (CH), 33.1 (CH), 28.1 (CH_2), 27.6 (CH_2), 25.1 (CH_3), 24.9 (CH_3), 19.7 (CH_3), 17.8 (CH_3), 12.3 (CH_3), 10.3 (CH_3). HRMS-ESI+ $[MH]^+$ Calc. for $C_{20}H_{34}BO_6$: 381.2442; found: 381.2442.

Dimethyl 3-isopropyl-4-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopent-2-ene-1,1-dicarboxylate (68a)



Following general borylative cyclization procedure, **68a** was obtained after 3 h (70 ºC) in 11% yield (calculated by NMR) as a colorless oil (hexane/EtOAc 20:1). Partial decomposition of the boronate was detected. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.40 (broad s, 1H), 3.70 (s, 3H), 3.70 (s, 3H), 2.81 (d, J = 13.4 Hz, 1H), 2.30 (sept, J = 6.8 Hz, 1H), 2.09 (d, J = 13.4 Hz, 1H), 1.19 (broad s, 12H), 1.13 (broad s, 3H), 1.08 (d, J = 6.8 Hz, 3H), 1.05 (d, J = 6.9 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.9 (C), 172.2 (C), 161.8 (C), 118.7 (CH), 83.5 (C), 65.1 (C), 52.7 (CH_3), 52.5 (CH_3), 44.1 (CH_2), 27.9 (CH), 24.9 (CH_3), 24.8 (CH_3), 23.3 (CH_3), 22.9 (CH_3), 22.6 (CH_3). HRMS-ESI+ $[M+Na]^+$ Calc. for $C_{19}H_{31}BO_6Na$: 389.2105; found: 389.2101.

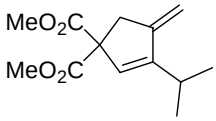
Dimethyl 3-sec-butyl-4-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopent-2-ene-1,1-dicarboxylate (68b)



Following general borylative cyclization procedure, **68b** was obtained after 16 h (50 ºC) in 31% yield (calculated by NMR) as a colorless oil (hexane/EtOAc 20:1). Mixture of two diasteroisomers (55:45). Partial decomposition of the boronate was detected. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.37 (broad s, 2H), 3.71 (s, 3H), 3.71 (s, 3H), 3.69 (s, 3H), 3.69 (s, 3H), 2.81 (d, J = 13.4 Hz, 1H), 2.80 (d, J = 13.4 Hz, 1H), 2.12 (d, J = 13.4 Hz, 1H), 2.11 (d, J = 13.4 Hz, 1H), 2.09-2.03 (m, 1H), 1.59-1.50 (m, 1H), 1.38-1.28 (m, 2H), 1.28-1.20 (m, 2H), 1.19 (broad s, 24H), 1.14 (s, 3H), 1.11 (s, 3H), 1.05 (d, J = 6.7

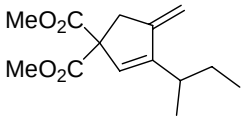
Hz, 3H), 1.04 (d, J = 6.8 Hz, 3H), 0.88 (t, J = 7.4 Hz, 3H), 0.87 (t, J = 7.4 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 173.0 (C), 172.8 (C), 172.5 (C), 160.9 (C), 160.7 (C), 119.1 (CH), 119.0 (CH), 83.5 (C), 83.5 (C), 65.1 (C), 52.8 (CH_3), 52.8 (CH_3), 52.6 (CH_3), 52.5 (CH_3), 43.9 (CH_2), 43.7 (CH_2), 34.6 (CH), 34.5 (CH), 30.1 (CH_2), 29.8 (CH_2), 25.0 (CH_3), 24.9 (CH_3), 24.8 (CH_3), 24.8 (CH_3), 22.9 (CH_3), 22.5 (CH_3), 20.8 (CH_3), 20.6 (CH_3), 12.2 (CH_3), 12.1 (CH_3). HRMS-ESI+ $[MH]^+$ Calc. for $C_{20}H_{34}BO_6$: 381.2442; found: 381.2449.

Dimethyl 3-isopropyl-4-methylenecyclopent-2-ene-1,1-dicarboxylate (69a)



Following general borylative cyclization procedure, **69a** was obtained after 3 h (70 ºC) in 20% yield as a colorless oil (hexane/EtOAc 20:1). This cycloisomerization product has been described previously in the literature.[287]

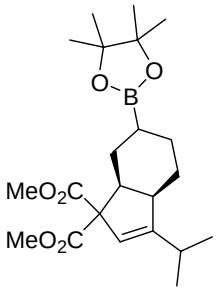
Dimethyl 3-*sec*-butyl-4-methylenecyclopent-2-ene-1,1-dicarboxylate (69b)



Following general borylative cyclization procedure, **69b** was obtained after 16 h (50 ºC) in 20% yield as a colorless oil (hexane/EtOAc 20:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.88 (broad s, 1H), 4.97-4.94 (m, 1H), 4.93-4.90 (m, 1H), 3.73 (broad s, 3H), 3.73 (broad s, 3H), 3.19-3.16 (m, 2H), 2.41-2.28 (m, 1H), 1.67-1.52 (m, 1H), 1.50-1.34 (m, 1H), 1.10 (d, J = 6.9 Hz, 3H), 0.87 (t, J = 7.4 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 171.6 (C), 171.5 (C), 153.6 (C), 150.0 (C), 129.0 (CH), 103.4 (CH_2), 63.4 (C), 53.0 (CH_3), 53.0 (CH_3), 38.7 (CH_2), 32.7 (CH), 28.8 (CH_2), 19.3 (CH_3), 11.7 (CH_3). HRMS-ESI+ $[MH]^+$ Calc. for $C_{14}H_{21}O_4$: 253.1460; found: 253.1461.

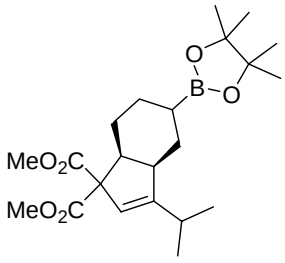
[287] Närhi, K.; Franzén, J.; Bäckvall, J-E. *Chem. Eur. J.* **2005**, *11*, 6937-6943.

Dimethyl 3-isopropyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3a,4,5,6,7,7a-hexahydroindene-1,1-dicarboxylate (71a)



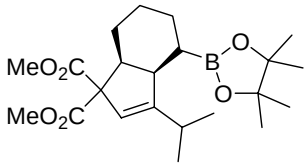
Following general borylative cyclization procedure, **71a** was obtained after 7 h (50 ºC) in 12% yield as a white solid (hexane/EtOAc 10:1). The relative configuration of the carbons involved in the fusion of the cycles were determinated by a NOESY experiment which showed NOE between the corresponding protons on the mentioned carbons. Partial decomposition of the boronate was detected. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.42 (broad s, 1H), 3.69 (s, 3H), 3.64 (s, 3H), 3.15-3.07 (m, 1H), 2.93 (dt, J = 12.1, 5.6 Hz, 1H), 2.25 (sept, J = 6.7 Hz, 1H), 1.93-1.82 (m, 1H), 1.61-1.43 (m, 2H), 1.43-1.33 (m, 1H), 1.17 (broad s, 12H), 1.12 (d, J = 6.7 Hz, 3H), 1.10-0.94 (m, 2H), 0.91 (d, J = 6.8 Hz, 3H), 0.87-0.74 (m, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 171.3 (C), 170.5 (C), 157.5 (C), 119.5 (CH), 83.0 (C), 68.5 (C), 52.5 (CH_3), 52.1 (CH_3), 45.2 (CH), 43.1 (CH), 27.4 (CH), 25.3 (CH_2), 25.2 (CH_2), 24.9 (CH_3), 24.8 (CH_3), 24.0 (CH_2), 21.7 (CH_3), 20.6 (CH_3). HRMS-ESI+ $[MH]^+$ Calc. for $C_{22}H_{36}BO_6$: 407.2599; found: 407.2597.

Dimethyl 3-isopropyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3a,4,5,6,7,7a-hexahydroindene-1,1-dicarboxylate (71b)



Following general borylative cyclization procedure, **71b** was obtained after 7 h (50 ºC) in 7% yield (10% yield calculated by NMR) as a white solid (hexane/EtOAc 10:1), mp 104-107 ºC. The relative configuration of the carbons involved in the fusion of the cycles were determinated by a NOESY experiment which showed NOE between the corresponding protons on the mentioned carbons. The relative configuration of the Bpin group has been also elucidated by a NOESY experiment. Partial decomposition of the boronate was detected. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.31 (m, 1H), 3.70 (s, 3H), 3.69 (s, 3H), 3.07-2.98 (m, 1H), 2.78-2.67 (m, 1H), 2.42 (sept, J = 6.8 Hz, 1H), 1.85-1.67 (m, 2H), 1.61-1.40 (m, 2H), 1.20 (s, 12H), 1.19-1.13 (m, 2H), 1.11 (d, J = 6.8 Hz, 3H), 0.96 (d, J = 6.8 Hz, 3H), 0.94-0.83 (m, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.3 (C), 171.9 (C), 160.2 (C), 119.1 (CH), 83.1 (C), 68.1 (C), 52.7 (CH_3), 52.3 (CH_3), 45.5 (CH), 42.5 (CH), 27.8 (CH_2), 27.5 (CH), 25.0 (CH_3), 24.8 (CH_3), 23.6 (CH_2), 23.3 (CH_2), 21.7 (CH_3), 20.8 (CH_3). HRMS-ESI+ $[MH]^+$ Calc. for $C_{22}H_{36}BO_6$: 407.2599; found: 407.2617.

Dimethyl 3-isopropyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3a,4,5,6,7,7a-hexahydroindene-1,1-dicarboxylate (71c)

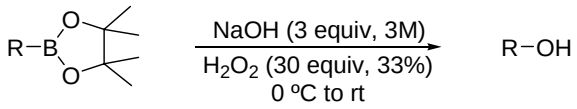


Following general borylative cyclization procedure, **71c** was obtained after 7 h (50 ºC) in 30% yield (33% yield calculated by NMR) as a white solid (hexane/EtOAc 10:1), mp 104-107 ºC. The relative configuration of the carbons involved in the fusion of the cycles were determinated by a NOESY experiment which showed NOE between the corresponding protons on the mentioned carbons. Partial decomposition of the boronate was detected. ^{1}H-NMR (300 MHz, $CDCl_3$ δ 5.52 (broad s, 1H), 3.70 (s, 3H), 3.65 (s, 3H), 3.47-3.44 (m, 1H), 2.93-2.88 (m, 1H), 2.12 (sept, J = 6.8 Hz, 1H), 1.69-1.59 (m, 2H), 1.36-1.26 (m, 2H), 1.23 (s, 6H), 1.21 (s, 6H), 1.21-1.13 (m, 3H), 1.12 (d, J = 6.8 Hz, 3H), 1.02 (d, J = 6.8 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 171.3 (C), 170.3 (C), 158.4 (C), 120.7 (CH), 83.3 (C), 68.0 (C), 52.5 (CH_3), 52.2 (CH_3), 46.1 (CH), 45.9 (CH), 27.5 (CH), 26.1 (CH_2), 25.2 (CH_3), 24.6 (CH_3), 24.2 (CH_2), 24.2

(CH_3), 23.7 (CH_2), 22.4 (CH_3). HRMS-ESI+ $[M+Na]^+$ Calc. for $C_{22}H_{35}BO_6Na$: 429.2418; found: 429.2415.

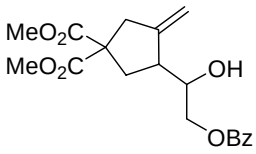
6. Alkyl- and allylboronates functionalizations

6.1 Oxidation and experimental data of resulting alcohols



Alcohols were preparated by standard conditions for oxidation of respective boronates. To a solution of boronate (*ca.* 50 mg) in THF (5 mL), an aqueous solution of NaOH (3M, 3 equiv) was added slowly at rt. Then, the mixture was cooled to 0 ºC and a solution of H_2O_2 (33% w/v, 30 equiv) was added dropwise. After addition the reaction was stirred at rt for 1-1.5 h. Then, water and Et_2O were added into the resulting mixture. The aqueous layer was separated and extracted with Et_2O (3 x 5 mL). The combined organic fractions were dried over anhydrous Mg_2SO_4 and filtered through anhydrous Na_2SO_4. The solvent was removed under vacuum and the residue was purified by column chromatography (hexane/EtOAc).

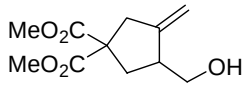
Dimethyl 3-(2-(benzoyloxy)-1-hydroxyethyl)-4-methylenecyclopentane-1,1-dicarboxylate (16)



Following general procedure for oxidation and starting from alkylboronate **2b**, secondary alcohol **16** was obtained after 1.5 h in 84% yield as a colorless oil (hexane/EtOAc 5:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.06 (m, 2H), 7.57 (m, 1H), 7.45 (m, 2H), 5.15 (c, J = 2.1 Hz, 1H), 5.01 (c, J = 2.1 Hz, 1H), 4.45-4.30 (m, 2H), 4.24 (m, 1H), 3.74 (s, 3H), 3.73 (s, 3H), 2.99 (m, 2H), 2.88 (m, 1H), 2.52 (m, 1H), 2.37 (m, 1H), 2.28 (d, J = 3.4 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.1 (C), 168.8

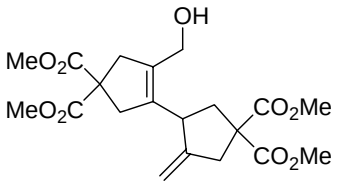
(C), 148.8 (C), 133.4 (CH), 130.0 (CH), 129.9 (CH), 128.6 (C), 108.6 (CH_2), 70.4 (CH), 67.4 (CH_2), 58.8 (C), 53.1 (CH_3), 45.5 (CH), 41.7 (CH_2), 33.5 (CH_2). HRMS-ESI+ $[M+Na]^+$ Calc. for $C_{19}H_{22}O_7Na$: 385.1257; found: 385.1254.

Dimethyl 3-(hydroxymethyl)-4-methylenecyclopentane-1,1-dicarboxylate (17)



Following general procedure for oxidation and starting from alkylboronate **2k**, primary alcohol **17** was obtained after 1.5 h in 93% yield as a colorless oil (hexane/EtOAc 1:2). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.04 (c, J = 2.2 Hz, 1H), 4.91 (c, J = 2.2 Hz, 1H), 3.71 (s, 3H), 3.70 (s, 3H), 3.65 (d, J = 0.6 Hz, 1H), 3.63 (d, J = 1.0 Hz, 1H), 3.03-2.88 (m, 2H), 2.78 (m, 1H), 2.58 (ddd, J = 13.2, 8.3, 0.8 Hz, 1H), 2.10 (dd, J = 13.4, 8.9 Hz, 1H), 1.80 (bs, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.3 (C), 172.2 (C), 148.9 (C), 108.1 (CH_2), 64.7 (CH_2), 58.8 (C), 53.0 (CH_3), 52.9 (CH_3), 44.9 (CH), 41.6 (CH_2), 36.9 (CH_2). HRMS-ESI+ $[MH]^+$ Calc. for $C_{11}H_{17}O_5$: 229.1070; found: 229.1072.

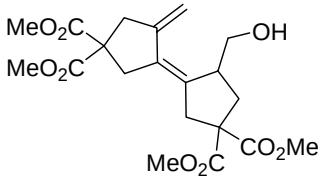
Dimethyl 3-(4,4-bis(methoxycarbonyl)-2-methylenecyclopentyl)-4-(hydroxymethyl)cyclopent-3-ene-1,1-dicarboxylate (36)



Following general procedure for oxidation and starting from allylboronate **26a**, primary allyl alcohol **36** was obtained after 1.5 h in 91% yield as a colorless oil (hexane/EtOAc 1:1.5). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.94 (c, J = 2.2 Hz, 1H), 4.61 (c, J = 2.4 Hz, 1H), 4.16 (s, 2H), 3.73 (s, 3H), 3.72 (s, 6H), 3.70 (s, 3H), 3.59 (m, 1H), 3.20 (d, J = 16.8 Hz, 1H), 3.08 (d, J = 17.9 Hz, 2H), 3.03-2.86 (m, 3H), 2.47 (ddd, J = 13.0, 7.7, 1.3 Hz, 1H), 2.05 (dd, J = 12.8, 12.0 Hz, 1H), 1.60 (bs, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.6 (C), 172.5 (C), 172.1 (C), 171.9 (C), 148.6 (C), 135.7 (C), 135.5 (C), 108.1 (CH_2), 58.8 (C), 58.4 (CH_2), 57.5 (C), 53.1 (CH_3), 53.0 (CH_3), 52.9 (CH_3), 42.2 (CH_2),

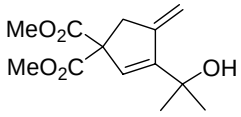
41.2 (CH), 40.4 (CH_2), 40.1 (CH_2), 38.4 (CH_2). HRMS-ESI+ $[M+NH_4]^+$ Calc. for $C_{20}H_{26}NO_9$: 428.1915; found: 428.1882.

Tetramethyl (1*Z*)-5-(hydroxymethyl)-5'-methylene-1,1'-bi(cyclopentylidene)-3,3,3',3'-tetracarboxylate (54)



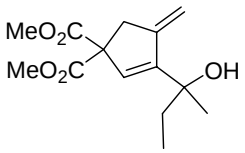
Following general procedure for oxidation and starting from alkylboronate **41a**, primary alcohol **54** was obtained after 1.5 h in 95% yield as a colorless oil (hexane/EtOAc 1:1.5). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.16 (s, 1H), 5.09 (s, 1H), 3.74 (s, 3H), 3.72 (s, 3H), 3.71 (s, 6H), 3.66 (dd, J = 11.1, 3.9 Hz, 1H), 3.46 (dd, J = 11.1, 8.1 Hz, 1H), 3.31 (m, 1H), 3.08-2.86 (m, 6H), 2.59-2.45 (m, 2H), 1.79 (bs, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.8 (C), 172.3 (C), 172.0 (C), 171.7 (C), 144.0 (C), 137.1 (C), 130.3 (C), 109.7 (CH_2), 62.2 (CH_2), 58.3 (C), 57.3 (C), 53.1 (CH_3), 53.0 (CH_3), 52.9 (CH_3), 44.1 (CH), 43.2 (CH_2), 41.3 (CH_2), 41.0 (CH_2), 37.1 (CH_2). HRMS-ESI+ $[MH]^+$ Calc. for $C_{20}H_{27}O_9$: 411.1649; found: 411.1640.

Dimethyl 3-(2-hydroxypropan-2-yl)-4-methylenecyclopent-2-ene-1,1-dicarboxylate (72a)



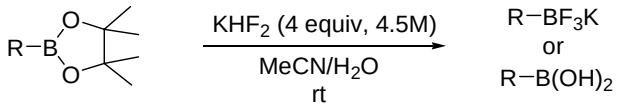
Following general procedure for oxidation and starting from allylboronate **61a**, quaternary allyl alcohol **72a** was obtained after 1 h in 99% yield as a yellowish oil (hexane/EtOAc 2:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 6.10 (broad s, 1H), 5.25 (t, J = 2.2 Hz, 1H), 5.07-5.04 (m, 1H), 3.72 (s, 6H), 3.20 (t, J = 2.0 Hz, 2H), 1.93 (broad s, 1H), 1.48 (s, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 171.1 (C), 154.3 (C), 146.9 (C), 130.5 (CH), 107.5 (CH_2), 70.8 (C), 62.5 (C), 53.1 (CH_3), 39.7 (CH_2), 29.6 (CH_3). HRMS-ESI+ $[M+Na]^+$ Calc. for $C_{13}H_{18}O_5Na$: 277.1046; found: 277.1040.

Dimethyl 3-(2-hydroxybutan-2-yl)-4-methylenecyclopent-2-ene-1,1-dicarboxylate (72b)



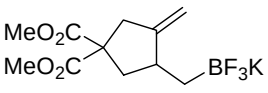
Following general procedure for oxidation and starting from allylboronate **61b**, quaternary allyl alcohol **72b** was obtained after 1 h in 98% yield as a yellowish oil (hexane/EtOAc 7:3). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 6.13 (broad s, 1H), 5.19 (t, J = 2.2 Hz, 1H), 5.05-5.01 (m, 1H), 3.73 (broad s, 6H), 3.21 (t, J = 2.0 Hz, 2H), 1.87-1.68 (m, 3H), 1.44 (s, 3H), 0.81 (t, J = 7.5 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 171.1 (C), 152.9 (C), 147.1 (C), 132.1 (CH), 107.0 (CH_2), 73.7 (C), 62.5 (C), 53.0 (CH_3), 39.9 (CH_2), 33.8 (CH_2), 27.8 (CH_3), 8.3 (CH_3). HRMS-ESI+ $[M+Na]^+$ Calc. for $C_{14}H_{20}O_5Na$: 291.1202; found: 291.1204.

6.2 Formation and experimental data of trifluoroborate salts and boronic acids



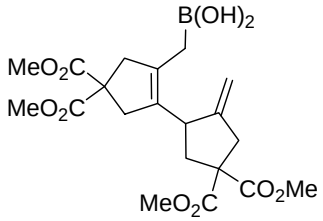
Trifloroborate salts were prepared following general procedure from respective boronates. To a solution of boronate (1 equiv) in acetonitrile at rt was added slowly a saturated aqueous solution of KHF_2 (4 equiv, 4.5 M). After indicated time at rt, the solvent was evaporated, and the remained white residue was washed successively with hot acetone to separate from inorganic impurities after filtration. The solvent was totally removed under vacuum and the white solid obtained washed with warm Et_2O and dried under vacuum line without further purification.

Potassium {[4,4-bis(methoxycarbonyl)-2-methylenecyclopentyl]methyl}(trifluoro)borate (18)



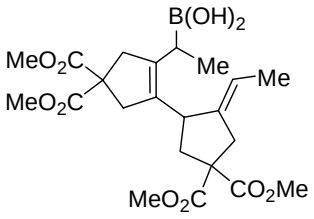
Following general procedure and starting from allylboronate **2k**, primary alkyl trifluoroborate salt **18** was obtained after 1.5 h in 85% yield as a white solid (mp 120-123 ºC). ^{1}H-NMR (300 MHz, Acetone-d^{6}) δ 4.78 (s, 1H), 4.72 (s, 1H), 3.66 (s, 3H), 3.65 (s, 3H), 2.96 (d, J = 16.7 Hz, 1H), 2.88-2.77 (m, 1H), 2.67 (dd, J = 12.8, 7.4 Hz, 1H), 2.43 (m, 1H), 1.68 (t, J = 12.4 Hz, 1H), 0.64 (m, 1H), 0.02 (m, 1H). ^{13}C-NMR (75 MHz, Acetone-d^{6}, DEPT-135) δ 173.9 (C), 173.7 (C), 104.2 (CH_2), 59.2 (C), 53.1 (CH_3), 53.0 (CH_3), 43.7 (CH_2), 41.7 (CH), 41.6 (CH_2), 24.2 (CH_2-B, HMQC). HRMS-ESI+ Calc. for $C_{12}H_{18}BO_5F_2$: 291.1220; found: 291.1233.

{[4,4,4',4'-Tetrakis(methoxycarbonyl)-2'-methylene-1,1'-bi(cyclopentan)-1-en-2-yl]methyl}boronic acid (38a)



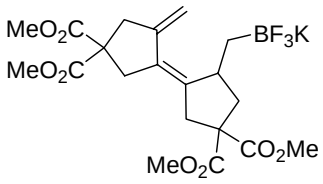
Following general procedure and starting from allylboronate **26a**, primary boronic acid **38a** was obtained after 1.5 h in 70% yield (calculated by NMR, mixed with free pinacol) as a sticky white solid. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.83 (s, 1H), 4.61 (s, 1H), 3.70 (s, 3H), 3.69 (s, 3H), 3.66 (s, 3H), 3.65 (s, 3H), 3.54 (m, 1H), 3.03-2.93 (m, 3H), 2.87-2.77 (m, 3H), 2.43 (dd, J = 12.7, 7.6 Hz, 1H), 1.90 (t, J = 12.6 Hz, 1H), 1.13 (m, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 173.9 (C), 173.6 (C), 173.0 (C), 172.2 (C), 149.3 (C), 139.0 (C), 125.6 (C), 107.0 (CH_2), 58.7 (C), 57.6 (C), 53.1 (CH_3), 52.9 (CH_3), 52.8 (CH_3), 52.7 (CH_3), 45.8 (CH_2), 42.3 (CH), 40.4 (CH_2), 39.5 (CH_2), 38.3 (CH_2), 19.1 (CH_2-B, HMQC). HRMS-ESI+ $[M+Na]^+$ Calc. for $C_{20}H_{27}BO_{10}Na$: 461.1589; found: 461.1589.

{1-[(2'*E*)-2'-Ethylidene-4,4,4',4'-tetrakis(methoxycarbonyl)-1,1'-bi(cyclopentan)-1-en-2-yl]ethyl}boronic acid (38b)



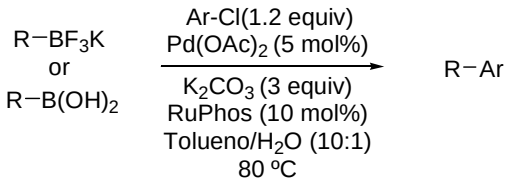
Following general procedure and starting from allylboronate **26b**, primary boronic acid **38b** was obtained after 1.5 h in 80% yield (calculated by NMR, mixed with free pinacol) as a sticky white solid. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.95 (m, 1H), 3.70 (s, 3H), 3.69 (s, 3H), 3.68 (s, 3H), 3.66 (s, 3H), 3.57 (m, 1H), 3.05-2.82 (m, 5H), 2.61 (d, J = 15.9 Hz, 1H), 2.47 (dd, J = 12.6, 7.0 Hz, 1H), 1.78 (t, J = 12.5 Hz, 1H), 1.55 (d, J = 6.6 Hz, 3H), 0.87 (m, 4H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 174.7 (C), 173.4 (C), 173.1 (C), 172.5 (C), 143.9 (C), 139.3 (C), 125.3 (C), 116.3 (CH), 58.7 (C), 57.3 (C), 53.0 (CH_3), 52.9 (CH_3), 52.8 (CH_3), 52.6 (CH_3), 42.6 (CH_2), 42.4 (CH), 39.2 (CH_2), 38.5 (CH_2), 37.2 (CH_2), 19.2 (CH-B, HMQC), 14.7 (CH_3), 13.9 (CH_3). HRMS-ESI+ $[M+Na]^+$ Calc. for $C_{22}H_{31}BO_{10}Na$: 489.1902; found: 489.1900.

Potassium trifluoro{[(1*Z*)-4,4,4',4'-tetrakis(methoxycarbonyl)-2'-methylene-1,1'-bi(cyclopentyliden)-2-yl]methyl}borate (55)



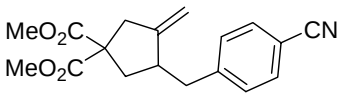
Following general procedure and starting from allylboronate **41a**, primary alkyl trifluoroborate salt **55** was obtained after 3 h in 80% yield as a white solid (mp 115-120 ºC). ^{1}H-NMR (300 MHz, Acetone-d^6) δ 5.32 (s, 1H), 4.97 (s, 1H), 3.68 (s, 6H), 3.67 (s, 3H), 3.64 (s, 3H), 3.13-3.68 (m, 7H), 2.58 (dd, J = 13.7, 8.2 Hz, 1H), 2.31 (dd, J = 13.6, 4.0 Hz, 1H), 0.60 (m, 1H), 0.02 (m, 1H). ^{13}C-NMR (75 MHz, Acetone-d^6, DEPT-135) δ 173.7 (C), 173.3 (C), 172.4 (C), 172.3 (C), 148.4 (C), 144.5 (C), 125.3 (C), 109.9 (CH_2), 59.4 (C), 58.3 (C), 53.0 (CH_3), 52.8 (CH_3), 44.2 (CH_2), 42.3 (CH_2), 41.5 (CH_2), 41.3 (CH_2), 39.2 (CH), 25.0 (CH_2-B, HMQC). HRMS-ESI+ Calc. for $C_{20}H_{25}BO_8F_3$: 461.1600; found: 461.1618.

6.3 Suzuki coupling and experimental data of resulting compounds



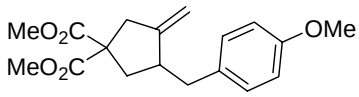
A reaction flask was charged with trifluoroborate salt or boronic acid (*ca.* 50 mg), $Pd(OAc)_2$ (5 mol%), RuPhos (10 mol%), K_2CO_3 (3 equiv), and respective aryl chloride (1.2 equiv) under Ar. To the flask were added toluene and H_2O (10:1) and the mixture was heated at 80 ºC. After indicated time, water and Et_2O were added into the resulting mixture. The aqueous layer was separated and extracted with Et_2O (3 x 5 mL). The combined organic fractions were dried over anhydrous Mg_2SO_4 and filtered through anhydrous Na_2SO_4. The solvent was removed under vacuum and the residue was purified by column chromatography (hexane/EtOAc).

Dimethyl 3-(4-cyanobenzyl)-4-methylenecyclopentane-1,1-dicarboxylate (19)



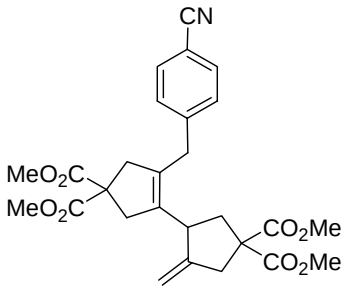
Following general procedure for Suzuki coupling and starting from trifluoroborate salt **18** and *p*-chloronitrile, coupling product **19** was obtained after 5 h in 71% yield as a white solid (hexane/EtOAc 8:1), mp 67-70 ºC. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.57 (d, J = 8.2 Hz, 2H), 7.30 (d, J = 8.2 Hz, 2H), 5.01 (d, J = 2.1 Hz, 1H), 4.84 (d, J = 2.1 Hz, 1H), 3.71 (s, 3H), 3.69 (s, 3H), 3.10-2.96 (m, 3H), 2.87 (m, 1H), 2.59 (dd, J = 13.6, 9.5 Hz, 1H), 2.35 (dd, J = 13.0, 7.7 Hz, 1H), 1.83 (dd, J = 13.0, 10.0 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.1 (C), 150.8 (C), 146.1 (C), 132.4 (CH), 129.9 (CH), 119.1 (C), 110.3 (C), 107.5 (CH_2), 58.3 (C), 53.0 (CH_3), 43.5 (CH), 41.1 (CH_2), 40.5 (CH_2), 39.7 (CH_2). HRMS-ESI+ $[MH]^+$ Calc. for $C_{18}H_{20}NO_4$: 314.1386; found: 314.1367.

Dimethyl 3-(4-methoxybenzyl)-4-methylenecyclopentane-1,1-dicarboxylate (20)



Following general procedure for Suzuki coupling and starting from trifluoroborate salt **18** and *p*-chloroanisol, coupling product **20** was obtained after 20 h in 50% yield as a colorless oil (hexane/EtOAc 2:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.10 (d, J = 8.6 Hz, 2H), 6.82 (d, J = 8.6 Hz, 2H), 4.98 (c, J = 2.2 Hz, 1H), 4.87 (c, J = 2.2 Hz, 1H), 3.79 (s, 3H), 3.71 (s, 3H), 3.69 (s, 3H), 3.09-2.91 (m, 3H), 2.82 (m, 1H), 2.46 (dd, J = 13.5, 9.4 Hz, 1H), 2.39 (ddd, J = 13.1, 7.7, 1.1 Hz, 1H), 1.86 (dd, J = 13.2, 10.0 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.4 (C), 172.3 (C), 158.1 (C), 151.6 (C), 132.5 (C), 130.0 (CH), 114.0 (CH), 106.9 (CH_2), 58.4 (C), 55.4 (CH_3), 52.9 (CH_3), 52.8 (CH_3), 44.1 (CH), 41.4 (CH_2), 39.9 (CH_2), 39.6 (CH_2). HRMS-ESI+ $[MH]^+$ Calc. for $C_{19}H_{23}O_5$: 319.1540; found: 319.1550.

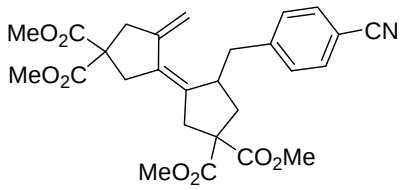
Dimethyl 3-(4,4-bis(methoxycarbonyl)-2-methylenecyclopentyl)-4-(4-cyanobenzyl)cyclopent-3-ene-1,1-dicarboxylate (39)



Following general procedure for Suzuki coupling and starting from boronic acid **38a** and *p*-chloronitrile, coupling product **39** was obtained after 4 h in 42% yield as a colorless oil (hexane/EtOAc 2:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.57 (d, J = 8.3 Hz, 2H), 7.23 (d, J = 8.3 Hz, 2H), 4.99 (c, J = 2.2 Hz, 1H), 4.66 (c, J = 2.4 Hz, 1H), 3.74 (s, 3H), 3.73 (s, 3H), 3.68 (s, 3H), 3.67 (s, 3H), 3.66 (m, 1H), 3.46 (s, 2H), 3.13-2.73 (m, 6H), 2.48 (ddd, J = 12.9, 7.6, 0.9 Hz, 1H), 2.07 (dd, J = 12.7, 11.9 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.4 (C), 172.2 (C), 171.8 (C), 148.5 (C), 144.8 (C), 134.9 (C), 133.5 (C), 132.5 (CH), 129.4 (CH), 119.1 (C), 110.4 (C), 108.3 (CH_2), 58.8

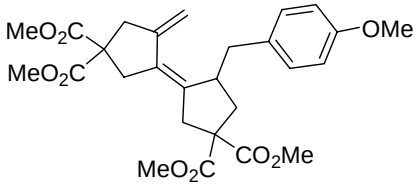
(C), 57.4 (C), 53.1 (CH_3), 53.0 (CH_3), 52.9 (CH_3), 52.8 (CH_3), 43.4 (CH_2), 42.1 (CH), 40.6 (CH_2), 39.6 (CH_2), 38.5 (CH_2), 34.6 (CH_2). HRMS-ESI+ $[MH]^+$ Calc. for $C_{27}H_{30}NO_8$: 469.1965; found: 469.1972.

Tetramethyl (1Z)-5-(4-cyanobenzyl)-5'-methylene-1,1'-bi(cyclopentylidene)-3,3,3',3'-tetracarboxylate (56)



Following general procedure for Suzuki coupling and starting from trifluoroborate salt **41a** and *p*-chloronitrile, coupling product **56** was obtained after 6 h in 67% yield as a colorless oil (hexane/EtOAc 3:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.58 (d, J = 8.2 Hz, 2H), 7.29 (d, J = 8.2 Hz, 2H), 5.20 (s, 1H), 5.16 (s, 1H), 3.76 (s, 3H), 3.75 (s, 3H), 3.74 (s, 3H), 3.70 (s, 3H), 3.36 (m, 1H), 3.17-2.91 (m, 7H), 2.41 (d, J = 14.0 Hz, 1H), 2.38 (dd, J = 13.9, 5.2 Hz, 1H), 2.16 (dd, J = 13.9, 3.9 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.7 (C), 172.0 (C), 171.9 (C), 171.7 (C), 145.9 (C), 144.5 (C), 140.0 (C), 132.4 (CH), 129.9 (CH), 129.4 (C), 119.1 (C), 110.3 (C), 109.6 (CH_2), 58.2 (C), 57.3 (C), 53.1 (CH_3), 53.0 (CH_3), 43.5 (CH_2), 42.2 (CH), 41.1 (CH_2), 38.5 (CH_2), 37.3 (CH_2). HRMS-ESI+ $[M+Na]^+$ Calc. for $C_{27}H_{29}NO_8Na$: 518.1785; found: 518.1770.

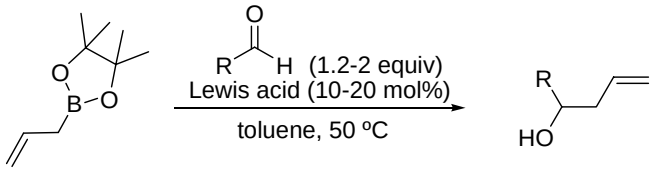
Tetramethyl (1Z)-5-(4-methoxybenzyl)-5'-methylene-1,1'-bi(cyclopentylidene)-3,3,3',3'-tetracarboxylate (57)



Following general procedure for Suzuki coupling and starting from trifluoroborate salt **41a** and *p*-chloroanisol, coupling product **57** was obtained after 20 h in less than 50% yield as a colorless oil (hexane/EtOAc 5:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.09 (d, J =

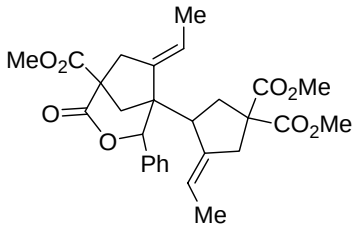
8.5 Hz, 2H), 6.83 (d, *J* = 8.5 Hz, 2H), 5.24 (s, 1H), 5.19 (s, 1H), 3.78 (s, 3H), 3.77 (s, 3H), 3.75 (s, 3H), 3.74 (s, 3H), 3.69 (s, 3H), 3.30 (m, 1H), 3.14-2.80 (m, 7H), 2.43 (dd, *J* = 13.9, 8.1 Hz, 1H), 2.23 (m, 2H). HRMS-ESI+ $[M+Na]^+$ Calc. for $C_{27}H_{32}O_9Na$: 523.1938; found: 523.1939.

6.4 Allylation and experimental data of resulting compounds



To a stirred solution of an allylboronate (*ca.* 50 mg) in anhydrous toluene (2 mL), under argon, was added respective Lewis acid (10-20 mol%) at r.t. Then, an aldehyde (1.2-2 equiv) was added and the reaction mixture was heated at 50 ºC. After indicated time, solvent was removed under vacuum and the reaction crude was purified by column cromatography (hexane/EtOAc).

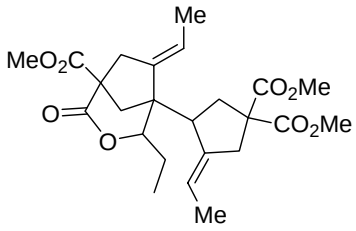
(*E*)-Dimethyl 3-ethylidene-4-((*E*)-7-ethylidene-5-(methoxycarbonyl)-4-oxo-2-phenyl-3-oxa-bicyclo[3.2.1]octan-1-yl)cyclopentane-1,1-dicarboxylate (37a)



Following general procedure for allylation and starting from allylboronate **26b** (0.091 mmol)**,** benzaldehyde (0.182 mmol) and $Sc(OTf)_3$ (20 mol%), lactone **37a** was obtained after 24 h in 83% yield as a crystalline white solid (hexane/EtOAc 3:1), mp 148-151 ºC. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.33-7.27 (m, 3H), 7.20-7.13 (m, 2H), 5.56 (s, 1H), 5.33 (m, 1H), 4.42 (m, 1H), 3.83 (s, 3H), 3.78 (s, 3H), 3.76 (s, 3H), 3.10-2.95 (m, 3H), 2.86 (dt, *J* = 17.2, 2.5 Hz, 1H), 2.75-2.60 (m, 2H), 2.48 (dd, *J* = 11.9, 1.8 Hz, 1H), 2.34 (d, *J* = 11.9 Hz, 1H), 2.08 (t, *J* = 12.3 Hz, 1H), 1.56-1.47 (m, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 171.9 (C), 171.7 (C), 170.4 (C), 170.2 (C), 137.0 (C), 135.7 (C),

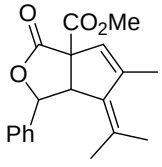
132.3 (C), 128.7 (CH), 128.0 (CH), 127.3 (CH), 124.7 (CH), 120.9 (CH), 89.6 (CH), 57.6 (C), 55.4 (C), 53.3 (C), 53.2 (CH_3), 53.1 (CH_3), 53.0 (CH_3), 42.2 (CH), 39.4 (CH_2), 38.2 (CH_2), 37.8 (CH_2), 36.4 (CH_2), 15.3 (CH_3), 14.3 (CH_3). HRMS-ESI+ $[MH]^+$ Calc. for $C_{28}H_{33}O_8$: 497.2169; found: 497.2165.

(*E*)-Dimethyl 3-((*E*)-2-ethyl-7-ethylidene-5-(methoxycarbonyl)-4-oxo-3-oxa-bicyclo[3.2.1]octan-1-yl)-4-ethylidenecyclopentane-1,1-dicarboxylate (37b)



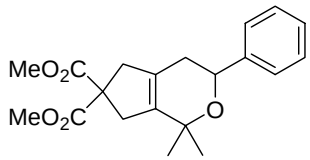
Following general procedure for allylation and starting from allylboronate **26b** (0.091 mmol)**,** propionaldehyde (0.182 mmol) and $Sc(OTf)_3$ (20 mol%), lactone **37b** was obtained after 24 h in 78% yield as a white solid (hexane/EtOAc 3:1), mp 142-145 ºC. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.49-5.32 (m, 2H), 4.15 (dd, J = 10.1, 2.0 Hz, 1H), 3.79 (s, 3H), 3.75 (s, 6H), 3.11-3.01 (m, 2H), 2.89 (d, J = 17.5 Hz, 1H), 2.77 (dt, J = 17.2, 2.6 Hz, 1H), 2.68 (dc, J = 17.0, 2.4 Hz, 1H), 2.43 (ddd, J = 12.3, 7.1, 1.9 Hz, 1H), 2.25 (d, J = 11.8 Hz, 1H), 2.19 (dd, J = 11.7, 1.5 Hz, 1H), 1.76 (t, J = 12.1 Hz, 1H), 1.68 (d, J = 6.8 Hz, 3H), 1.60-1.54 (m, 5H), 1.06 (t, J = 7.5 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 171.9 (C), 171.8 (C), 170.6 (C), 170.1 (C), 137.5 (C), 135.9 (C), 122.3 (CH), 120.5 (CH), 90.9 (CH), 57.8 (C), 55.5 (C), 53.2 (CH_3), 53.1 (CH_3), 52.9 (CH_3), 51.6 (C), 42.2 (CH), 39.7 (CH_2), 38.3 (CH_2), 36.9 (CH_2), 36.1 (CH_2), 22.8 (CH_2), 15.3 (CH_3), 14.6 (CH_3), 10.5 (CH_3). HRMS-ESI+ $[MH]^+$ Calc. for $C_{24}H_{33}O_8$: 449.2169; found: 449.2174.

Methyl 5-methyl-3-oxo-1-phenyl-6-(propan-2-ylidene)-3,3a,6,6a-tetrahydro-1H-cyclopenta[c]furan-3a-carboxylate (73)



Following general procedure for allylation and starting from allylboronate **61a** (0.140 mmol)**,** benzaldehyde (0.210 mmol) and $Y(OTf)_3$ (10 mol%) or $BF_3 \cdot Et_2O$ (20 mol%, lactone **73** was obtained after 40-48 h in 27% yield as a yellowish oil (hexane/EtOAc 15:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.42-7.31 (m, 2H), 7.24-7.19 (m, 1H), 7.09-7.03 (m, 2H), 5.87-5.78 (m, 1H), 4.40 (d, J = 10.0 Hz, 1H), 3.81 (s, 3H), 1.78 (d, J = 1.3 Hz, 3H), 1.61-1.48 (m, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 173.4 (C), 169.8 (C), 146.4 (C), 136.7 (C), 135.9 (C), 131.1 (C), 128.6 (CH), 127.8 (CH), 127.5 (CH), 127.0 (CH), 84.3 (CH), 64.5 (C), 53.4 (CH_3), 52.5 (CH), 25.7 (CH_3), 19.8 (CH_3), 17.9 (CH_3). HRMS-ESI+ $[MH]^+$ Calc. for $C_{19}H_{21}O_4$: 313.1434; found: 313.1425.

Dimethyl 1,1-dimethyl-3-phenyl-3,4-dihydrocyclopenta[c]pyran-6,6(1H,5H,7H)-dicarboxylate (74)



Following general procedure for allylation and starting from allylboronate **61a** (0.082 mmol)**,** benzaldehyde (0.100 mmol) and $BF_3 \cdot Et_2O$ (20 mol%, heterocyclic compound **74** was obtained after 40 h in 25% yield as a yellowish oil (hexane/EtOAc 7:1). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.40-7.37 (m, 2H), 7.36-7.31 (m, 2H), 7.28-7.26 (m, 1H), 4.66 (dd, J = 10.1, 3.7 Hz, 1H), 3.77 (s, 3H), 3.76 (s, 3H), 3.11-2.95 (m, 4H), 2.25-2.11 (m, 2H), 1.35 (s, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$, DEPT-135) δ 172.8 (C), 142.3 (C), 137.9 (C), 129.3 (C), 128.6 (CH), 127.5 (CH), 126.3 (CH), 74.5 (C), 70.9 (CH), 58.1 (C), 53.1 (CH_3), 43.8 (CH_2), 40.5 (CH_2), 33.9 (CH_2), 27.9 (CH_3), 24.4 (CH_3). HRMS-ESI+ $[M+Na]^+$ Calc. for $C_{20}H_{24}O_5Na$: 367.1515; found: 367.1528.

Appendix I:

COMPUTATIONAL SECTION

Contents ***Page***

Computational methods[†]

Calculations were performed with Gaussian 03 at DFT level.[288] The geometries of all complexes here reported were optimized using the B3LYP hybrid functional.[289] Optimizations were carried out using the standard 6-31G(d) basis set for C, H, and O. The LANL2DZ basis set, which includes the relativistic effective core potential (ECP) of Hay and Wadt and employs a split-valence (double-ζ) basis set, was used for Pd.[290] Harmonic frequencies were calculated at the same level to characterize the stationary points and to determine the zero-point energies (ZPE). The starting approximate geometries for the transition states (TS) were graphically located. Intrinsic reaction coordinate (IRC) studies were performed to confirm the relation of the transition states with the corresponding minima. All the calculations have been carried out in gas-phase.

[†] The computational studies have been performed by Dr. D. J. Cárdenas and Dr. Elena Buñuel.

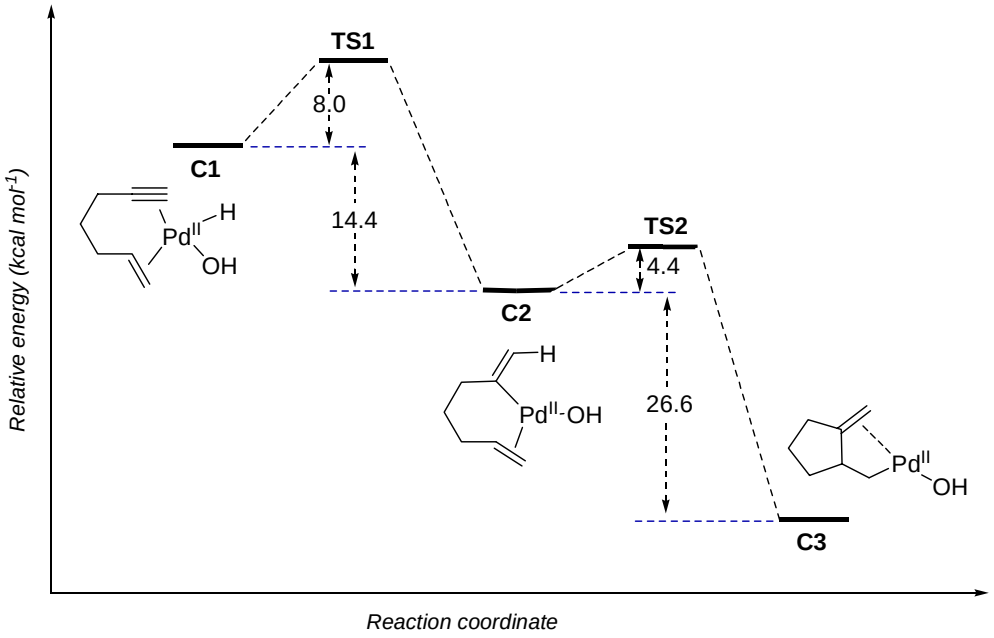
[288] Gaussian 03, Revision B.03, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery, Jr., T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez, and J. A. Pople, Gaussian, Inc., Pittsburgh PA, 2003.

[289] (a) Stephens, P. J.; Devlin, F. J.; Chabalowski, C. F.; Frisch, M. J. *J. Phys. Chem.* **1994**, *98*, 11623-11627. (b) Kohn, W.; Becke, A. D.; Parr, R. G. *J. Phys. Chem.* **1996**, *100*, 12974-12980. (c) Hay, P. J.; Wadt, W. R. *J. Chem. Phys.* **1985**, *82*, 270-283. (d) Hay, P. J.; Wadt, W. R. *J. Chem. Phys.* **1985**, *82*, 284-298. (e) Hay, P. J.; Wadt, W. R. *J. Chem. Phys.* **1985**, *82*, 299-310.

[290] (a) Becke, A. D. *J. Chem. Phys*. **1993**, *98*, 5648- 5653. (b) Becke, A. D. *Phys. Rev. A* **1988**, *38*, 3098-3100. (c) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785-789

1. Studies on the Mechanistic Pathways of Enynes

1.1 Alkyne Insertion into Pd–Hydride (Scheme 12)



C1

```
Zero-point correction=                           0.170479
(Hartree/Particle)
 Thermal correction to Energy=                    0.182032
 Thermal correction to Enthalpy=                  0.182976
 Thermal correction to Gibbs Free Energy=         0.133354
 Sum of electronic and zero-point Energies=           -475.658634
 Sum of electronic and thermal Energies=              -475.647081
 Sum of electronic and thermal Enthalpies=            -475.646137
 Sum of electronic and thermal Free Energies=         -475.695758
```

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	-0.112053	-1.854631	1.092111
2	6	0	-0.987906	-1.441542	0.322583
3	6	0	-2.243892	-1.144949	-0.390364
4	6	0	-2.385946	0.303140	-0.909513
5	6	0	-2.066695	1.386783	0.144826
6	6	0	-0.603577	1.749199	0.228769
7	6	0	0.168025	1.666092	1.334335
8	46	0	0.902661	-0.319360	-0.089884
9	8	0	2.226347	0.949950	-0.799034
10	1	0	1.649084	-1.484880	-0.791397
11	1	0	0.419631	-2.435026	1.817911
12	1	0	-2.344601	-1.842010	-1.232593
13	1	0	-3.071475	-1.365075	0.299201
14	1	0	-3.418059	0.419409	-1.260442
15	1	0	-1.736679	0.440710	-1.782255
16	1	0	-2.615034	2.300894	-0.123466
17	1	0	-2.440078	1.078968	1.130386
18	1	0	-0.166821	2.187368	-0.667787

19	1	0	1.186490	2.040425	1.332329
20	1	0	-0.225547	1.281489	2.272883
21	1	0	2.822166	0.484150	-1.404305

TS1

-638.6762
Zero-point correction= 0.168763
(Hartree/Particle)
Thermal correction to Energy= 0.180007
Thermal correction to Enthalpy= 0.180951
Thermal correction to Gibbs Free Energy= 0.131827
Sum of electronic and zero-point Energies= -475.645801
Sum of electronic and thermal Energies= -475.634557
Sum of electronic and thermal Enthalpies= -475.633613
Sum of electronic and thermal Free Energies= -475.682737

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	-0.004562	2.316899	0.086641
2	6	0	0.911787	1.460964	0.179851
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4	6	0	2.690457	-0.202638	-0.551046
5	6	0	2.059361	-1.500189	-0.013580
6	6	0	0.582381	-1.698855	-0.255622
7	6	0	-0.325458	-1.916561	0.739213
8	46	0	-0.849233	0.251398	-0.003019
9	8	0	-2.580762	-0.747571	-0.337271
10	1	0	-1.579659	1.667887	-0.159769
11	1	0	-0.387557	3.318343	0.052359
12	1	0	2.955857	1.889772	-0.050122
13	1	0	2.572560	0.864137	1.329472
14	1	0	3.781929	-0.310627	-0.529309
15	1	0	2.407710	-0.047268	-1.599820
16	1	0	2.575845	-2.346494	-0.489498
17	1	0	2.264971	-1.578423	1.062577
18	1	0	0.278585	-1.874947	-1.287388
19	1	0	-1.337080	-2.245065	0.528161
20	1	0	-0.017454	-1.871312	1.782509
21	1	0	-3.263430	-0.097085	-0.556010

C2

Zero-point correction= 0.174168
(Hartree/Particle)
Thermal correction to Energy= 0.185082
Thermal correction to Enthalpy= 0.186026
Thermal correction to Gibbs Free Energy= 0.137097
Sum of electronic and zero-point Energies= -475.681614
Sum of electronic and thermal Energies= -475.670701
Sum of electronic and thermal Enthalpies= -475.669756
Sum of electronic and thermal Free Energies= -475.718685

Center	Atomic	Atomic	Coordinates (Angstroms)

Number	Number	Type	X	Y	Z
1	6	0	0.468028	2.548923	0.226800
2	6	0	0.884335	1.277273	0.205050
3	6	0	2.319954	0.837819	0.168522
4	6	0	2.579050	-0.462961	-0.601886
5	6	0	1.846237	-1.655832	0.038456
6	6	0	0.353900	-1.682248	-0.174336
7	6	0	-0.580791	-1.714596	0.867080
8	46	0	-0.798711	0.202021	-0.045189
9	8	0	-2.764720	-0.192831	-0.298427
10	1	0	-0.586317	2.814524	0.349581
11	1	0	1.146540	3.399035	0.116359
12	1	0	2.932981	1.646270	-0.256820
13	1	0	2.674790	0.700034	1.202070
14	1	0	3.656311	-0.669656	-0.608148
15	1	0	2.268654	-0.350899	-1.649463
16	1	0	2.247354	-2.590005	-0.380289
17	1	0	2.064841	-1.672102	1.114402
18	1	0	0.027409	-2.021809	-1.157850
19	1	0	-1.591399	-2.082221	0.709960
20	1	0	-0.244193	-1.617855	1.897588
21	1	0	-2.962783	-0.195877	-1.249403

TS2

-296.0533
Zero-point correction= 0.174725
(Hartree/Particle)
Thermal correction to Energy= 0.184753
Thermal correction to Enthalpy= 0.185697
Thermal correction to Gibbs Free Energy= 0.138990
Sum of electronic and zero-point Energies= -475.674529
Sum of electronic and thermal Energies= -475.664502
Sum of electronic and thermal Enthalpies= -475.663557
Sum of electronic and thermal Free Energies= -475.710264

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	-0.920600	1.949139	1.107368
2	6	0	-0.952907	0.971810	0.187848
3	6	0	-1.949258	0.864766	-0.935961
4	6	0	-2.865439	-0.320925	-0.589094
5	6	0	-1.950186	-1.466143	-0.131607
6	6	0	-0.880781	-0.961417	0.827910
7	6	0	0.417165	-1.600699	0.821309
8	46	0	0.979309	0.137856	-0.082593
9	8	0	2.882291	0.000373	-0.562257
10	1	0	-0.290195	1.897434	1.991708
11	1	0	-1.505720	2.860683	0.980962
12	1	0	-2.517213	1.798048	-1.038286
13	1	0	-1.440855	0.678961	-1.890972
14	1	0	-3.492236	-0.623398	-1.435189
15	1	0	-3.534880	-0.029636	0.230544
16	1	0	-2.524473	-2.259556	0.364613
17	1	0	-1.456130	-1.918626	-1.000299
18	1	0	-1.244998	-0.666009	1.809440
19	1	0	0.962417	-1.688114	1.759732

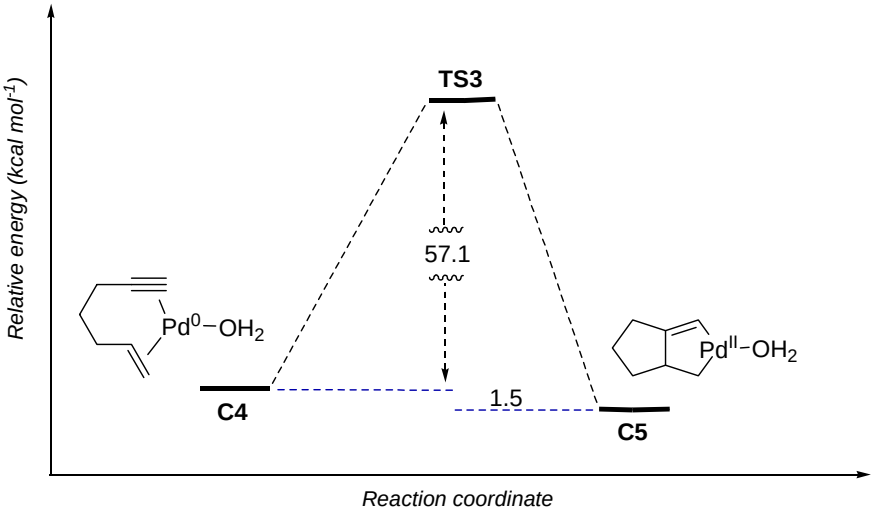
20	1	0	0.581474	-2.427049	0.129722
21	1	0	2.968300	-0.586287	-1.331295

C3

Zero-point correction= 0.174168
(Hartree/Particle)
Thermal correction to Energy= 0.185082
Thermal correction to Enthalpy= 0.186026
Thermal correction to Gibbs Free Energy= 0.137097
Sum of electronic and zero-point Energies= -475.681614
Sum of electronic and thermal Energies= -475.670701
Sum of electronic and thermal Enthalpies= -475.669756
Sum of electronic and thermal Free Energies= -475.718685

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	-0.267204	1.663588	0.968910
2	6	0	-1.047758	0.726563	0.336116
3	6	0	-1.947086	0.944911	-0.873315
4	6	0	-3.057507	-0.109120	-0.673927
5	6	0	-2.307515	-1.314870	-0.075580
6	6	0	-1.276692	-0.693914	0.897052
7	6	0	0.121014	-1.306883	0.874288
8	46	0	1.114511	0.201669	-0.082514
9	8	0	2.710833	-0.788413	-0.653089
10	1	0	0.096368	1.509822	1.982478
11	1	0	-0.195408	2.679057	0.586851
12	1	0	-2.318428	1.973906	-0.925925
13	1	0	-1.406520	0.746134	-1.806885
14	1	0	-3.585515	-0.350196	-1.601980
15	1	0	-3.801974	0.265254	0.040825
16	1	0	-2.969308	-2.032359	0.419438
17	1	0	-1.779910	-1.852446	-0.874164
18	1	0	-1.689332	-0.645433	1.914975
19	1	0	0.615733	-1.406308	1.842448
20	1	0	0.239415	-2.210758	0.275706
21	1	0	2.537187	-1.107773	-1.554672

1.2 Oxidative Cyclometalation (Scheme 13)



C4

```
 Zero-point correction=                           0.172655
(Hartree/Particle)
 Thermal correction to Energy=                    0.185014
 Thermal correction to Enthalpy=                  0.185958
 Thermal correction to Gibbs Free Energy=         0.133791
 Sum of electronic and zero-point Energies=           -475.703498
 Sum of electronic and thermal Energies=              -475.691139
 Sum of electronic and thermal Enthalpies=            -475.690195
 Sum of electronic and thermal Free Energies=         -475.742361
```

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	46	0	-0.686192	-0.080629	-0.016082
2	6	0	-0.299645	-2.180862	-0.075505
3	6	0	0.780316	-1.546118	0.089532
4	6	0	0.749618	1.602786	-0.403656
5	6	0	-0.324936	2.116303	0.297705
6	6	0	2.225026	-1.300250	0.303568
7	6	0	2.769145	-0.001062	-0.326718
8	6	0	2.111075	1.298544	0.181829
9	1	0	-0.796278	-3.126838	-0.207777
10	1	0	0.732618	1.681245	-1.492018
11	1	0	-0.260572	2.288369	1.370307
12	1	0	-1.143893	2.607662	-0.221589
13	1	0	2.796863	-2.153884	-0.087580
14	1	0	2.416750	-1.271784	1.386243
15	1	0	3.845597	0.041313	-0.116832
16	1	0	2.665287	-0.057526	-1.418526
17	1	0	2.051520	1.284905	1.278158
18	1	0	2.779321	2.133356	-0.082729
19	8	0	-3.136190	0.147069	-0.038986
20	1	0	-3.260134	-0.202406	0.858573
21	1	0	-3.236327	-0.628089	-0.615099

TS3

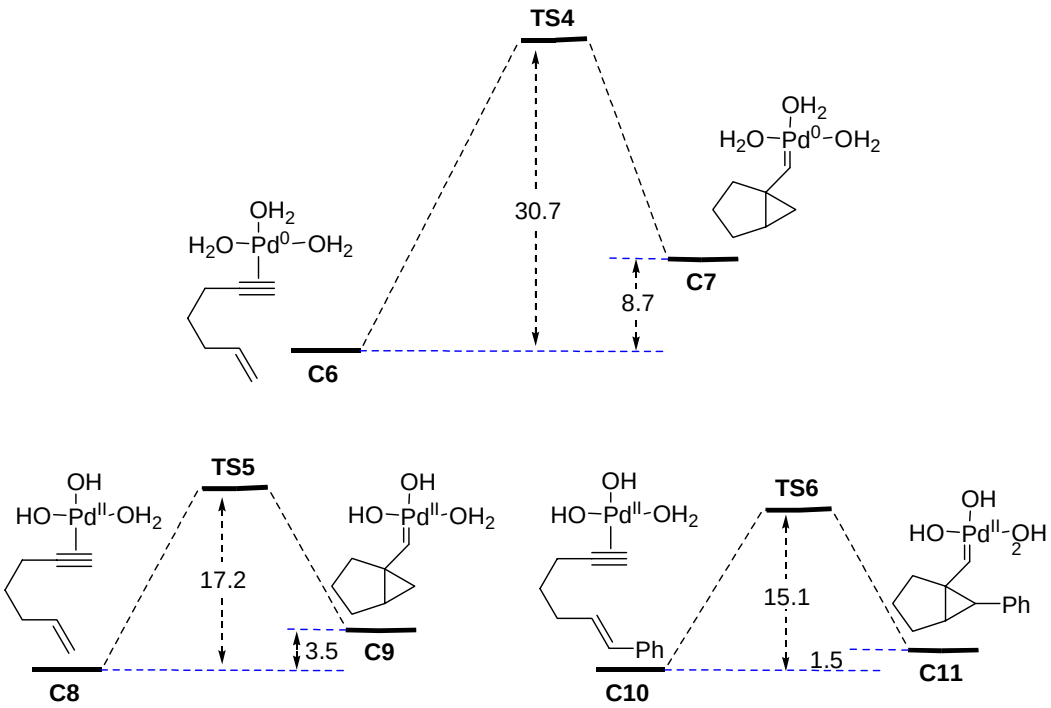
```
-713.1226
 Zero-point correction=                           0.172277
(Hartree/Particle)
 Thermal correction to Energy=                    0.183426
 Thermal correction to Enthalpy=                  0.184370
 Thermal correction to Gibbs Free Energy=         0.134996
 Sum of electronic and zero-point Energies=           -475.612551
 Sum of electronic and thermal Energies=              -475.601402
 Sum of electronic and thermal Enthalpies=            -475.600458
 Sum of electronic and thermal Free Energies=         -475.649832
---------------------------------------------------------------------
 Center     Atomic     Atomic              Coordinates (Angstroms)
 Number     Number      Type              X           Y           Z
 ---------------------------------------------------------------------
    1         46             0       -1.145470    0.218108    0.004009
    2          6             0       -0.140490   -1.513190   -0.078564
    3          6             0        1.065422   -1.080856   -0.128626
    4          6             0        1.236801    0.930800   -0.373390
    5          6             0        0.210734    1.928396   -0.066644
    6          6             0        2.487220   -1.522589    0.019011
    7          6             0        3.396412   -0.272153   -0.026260
    8          6             0        2.543392    0.917248    0.414450
    9          1             0       -0.750055   -2.404771   -0.019094
   10          1             0        1.398424    0.814467   -1.447551
   11          1             0        0.311349    2.437565    0.891004
   12          1             0       -0.061060    2.585653   -0.889339
   13          1             0        2.763848   -2.254013   -0.751448
   14          1             0        2.593010   -2.032365    0.986160
   15          1             0        4.285285   -0.403075    0.599905
   16          1             0        3.749218   -0.101046   -1.051580
   17          1             0        2.327919    0.878337    1.490068
   18          1             0        3.055390    1.871445    0.225238
   19          8             0       -3.096778   -0.862312    0.122158
   20          1             0       -3.532635   -0.453754   -0.646185
   21          1             0       -3.471782   -0.398854    0.891264
 ---------------------------------------------------------------------
```

C5

```
 Zero-point correction=                           0.176051
(Hartree/Particle)
 Thermal correction to Energy=                    0.186838
 Thermal correction to Enthalpy=                  0.187782
 Thermal correction to Gibbs Free Energy=         0.139005
 Sum of electronic and zero-point Energies=           -475.705823
 Sum of electronic and thermal Energies=              -475.695036
 Sum of electronic and thermal Enthalpies=            -475.694092
 Sum of electronic and thermal Free Energies=         -475.742869
---------------------------------------------------------------------
 Center     Atomic     Atomic              Coordinates (Angstroms)
 Number     Number      Type              X           Y           Z
 ---------------------------------------------------------------------
    1          6             0       -2.582796    1.504853   -0.084958
    2          6             0       -1.510374   -0.687827    0.398890
    3          6             0       -2.919899   -0.932748   -0.185236
    4          6             0       -3.654795    0.394313    0.117035
    5          6             0        0.003438    1.127086   -0.155689
    6          6             0       -1.264055    0.762252    0.078595
```

7	6	0	-0.305233	-1.488819	-0.130249
8	46	0	1.363192	-0.314119	-0.014310
9	8	0	3.292637	0.972495	0.108229
10	1	0	-2.705448	2.328035	0.630256
11	1	0	-2.655713	1.947718	-1.087137
12	1	0	-1.567969	-0.810668	1.492571
13	1	0	-3.429002	-1.807402	0.235420
14	1	0	-2.843944	-1.082678	-1.271454
15	1	0	-3.991115	0.393553	1.161936
16	1	0	-4.543770	0.545568	-0.505260
17	1	0	0.309373	2.125551	-0.480768
18	1	0	-0.120036	-2.424331	0.415086
19	1	0	-0.427442	-1.716428	-1.197150
20	1	0	3.248612	1.534462	-0.683000
21	1	0	3.080812	1.561457	0.851591

1.3 Cyclopropyl Carbenes (Scheme 14)



C6

Zero-point correction= 0.223096
(Hartree/Particle)
Thermal correction to Energy= 0.241506
Thermal correction to Enthalpy= 0.242450
Thermal correction to Gibbs Free Energy= 0.173413
Sum of electronic and zero-point Energies= -628.494704
Sum of electronic and thermal Energies= -628.476294
Sum of electronic and thermal Enthalpies= -628.475350
Sum of electronic and thermal Free Energies= -628.544387

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z

1	46	0	-1.056506	-0.200925	-0.189749
2	6	0	0.398832	-0.450247	1.257346
3	6	0	0.926680	-0.792527	0.170265
4	6	0	1.927986	-1.330324	-0.777149
5	6	0	3.350427	-1.475038	-0.185593
6	6	0	4.196256	-0.185563	-0.193868
7	6	0	3.667645	0.942532	0.650456
8	6	0	3.460680	2.188520	0.220433
9	8	0	-3.801715	-1.436737	0.952164
10	8	0	-3.044578	0.354841	-0.991111
11	1	0	0.383683	-0.254490	2.313571
12	1	0	1.576234	-2.314339	-1.114070
13	1	0	1.962202	-0.702673	-1.677142
14	1	0	3.276847	-1.871414	0.835126
15	1	0	3.885838	-2.230915	-0.774457
16	1	0	5.202497	-0.453529	0.164377
17	1	0	4.320393	0.161457	-1.228700
18	1	0	3.468324	0.702376	1.696032
19	1	0	3.099538	2.970735	0.882849
20	1	0	3.647748	2.474899	-0.812943
21	1	0	-3.785391	-0.954015	1.794562
22	1	0	-2.857049	-1.649071	0.795217
23	1	0	-3.622381	-0.180368	-0.397024
24	1	0	-3.090963	1.289719	-0.680554
25	8	0	-2.277631	2.766752	0.085957
26	1	0	-1.565400	2.153138	0.370117
27	1	0	-1.882471	3.238090	-0.665935

TS4

-452.9192
Zero-point correction= 0.223401
(Hartree/Particle)
Thermal correction to Energy= 0.240365
Thermal correction to Enthalpy= 0.241309
Thermal correction to Gibbs Free Energy= 0.176227
Sum of electronic and zero-point Energies= -628.445750
Sum of electronic and thermal Energies= -628.428786
Sum of electronic and thermal Enthalpies= -628.427842
Sum of electronic and thermal Free Energies= -628.492924

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	1.550168	-0.317669	0.103381
2	6	0	3.706781	-0.678488	-0.610733
3	6	0	4.172278	0.714959	-0.291628
4	6	0	3.403696	1.236801	0.934959
5	6	0	1.889904	0.988584	0.761072
6	6	0	3.238899	-1.534637	0.346872
7	6	0	0.621080	-0.973063	-0.531771
8	46	0	-1.255519	-0.363453	-0.471243
9	8	0	-3.118880	-1.076091	1.993384
10	8	0	-2.033975	2.654427	-0.084620
11	8	0	-3.419342	0.262771	-0.421671
12	1	0	3.659104	-0.981709	-1.653606
13	1	0	3.997197	1.362445	-1.159570
14	1	0	5.255807	0.736384	-0.103232
15	1	0	3.765747	0.733850	1.838622

16	1	0	3.589247	2.305414	1.083978
17	1	0	1.460624	1.788461	0.146222
18	1	0	1.394765	1.045278	1.737874
19	1	0	2.899781	-2.529846	0.081230
20	1	0	3.392540	-1.364774	1.407570
21	1	0	0.799614	-1.902189	-1.071626
22	1	0	-2.335104	-1.327466	1.451889
23	1	0	-2.764187	-0.379829	2.570440
24	1	0	-1.955059	2.906588	-1.019834
25	1	0	-1.399932	1.898561	-0.007367
26	1	0	-3.648415	-0.140215	0.448505
27	1	0	-3.277140	1.220124	-0.243566

C7

Zero-point correction= 0.226049
(Hartree/Particle)
Thermal correction to Energy= 0.242761
Thermal correction to Enthalpy= 0.243705
Thermal correction to Gibbs Free Energy= 0.179034
Sum of electronic and zero-point Energies= -628.480828
Sum of electronic and thermal Energies= -628.464117
Sum of electronic and thermal Enthalpies= -628.463172
Sum of electronic and thermal Free Energies= -628.527844

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	1.877799	-0.572362	-0.049830
2	6	0	3.036377	-0.207197	-1.066787
3	6	0	3.894785	0.847096	-0.384174
4	6	0	3.639621	0.673694	1.130464
5	6	0	2.176416	0.187969	1.242503
6	6	0	2.974738	-1.569053	-0.504021
7	6	0	0.554210	-0.715046	-0.585299
8	46	0	-1.095700	-0.043196	0.067325
9	8	0	-3.624608	-1.906266	-0.186124
10	8	0	-3.151088	0.544843	0.811034
11	1	0	2.772114	-0.066215	-2.110885
12	1	0	3.569258	1.838887	-0.720480
13	1	0	4.956140	0.745922	-0.644436
14	1	0	4.326573	-0.073612	1.544696
15	1	0	3.815228	1.600199	1.685788
16	1	0	1.481919	1.033020	1.300530
17	1	0	2.007822	-0.431568	2.131259
18	1	0	2.650290	-2.377831	-1.152249
19	1	0	3.685217	-1.869562	0.262172
20	1	0	0.585614	-1.276289	-1.531510
21	1	0	-3.359703	-2.565191	0.477546
22	1	0	-2.766603	-1.669035	-0.613180
23	1	0	-3.140905	0.601581	1.779505
24	1	0	-3.602029	-0.309781	0.569617
25	8	0	-2.124039	2.702100	-1.001967
26	1	0	-1.545035	1.983633	-1.314544
27	1	0	-2.759518	2.226855	-0.441486

C8

```
Zero-point correction=                           0.200828
(Hartree/Particle)
 Thermal correction to Energy=                    0.216947
 Thermal correction to Enthalpy=                  0.217892
 Thermal correction to Gibbs Free Energy=         0.155331
 Sum of electronic and zero-point Energies=           -627.266054
 Sum of electronic and thermal Energies=              -627.249935
 Sum of electronic and thermal Enthalpies=            -627.248991
 Sum of electronic and thermal Free Energies=         -627.311552

---------------------------------------------------------------------
 Center     Atomic     Atomic              Coordinates (Angstroms)
 Number     Number      Type              X           Y           Z
 ---------------------------------------------------------------------
    1         46              0       -1.491714   -0.000846    0.092883
    2          6              0        0.361471    0.536938    1.213060
    3          6              0        0.837013   -0.177444    0.333022
    4          6              0        1.489931   -1.140288   -0.560672
    5          6              0        2.910689   -1.554866   -0.111493
    6          6              0        4.022155   -0.529939   -0.413061
    7          6              0        3.909583    0.771100    0.335096
    8          6              0        3.884492    1.980676   -0.227715
    9          8              0       -1.362043   -1.936226    0.321847
   10          8              0       -2.082574    2.092505   -0.287013
   11          8              0       -3.410130   -0.049302   -0.526622
   12          1              0        0.212498    1.211022    2.029963
   13          1              0        0.832699   -2.018483   -0.581086
   14          1              0        1.521578   -0.738395   -1.582179
   15          1              0        2.894411   -1.793518    0.959086
   16          1              0        3.153484   -2.488006   -0.634320
   17          1              0        4.982142   -1.004031   -0.157703
   18          1              0        4.053604   -0.330801   -1.492896
   19          1              0        3.862811    0.691118    1.422695
   20          1              0        3.820240    2.888242    0.366571
   21          1              0        3.933820    2.109822   -1.307399
   22          1              0       -2.298323   -2.201390    0.308680
   23          1              0       -1.675204    2.389294   -1.117903
   24          1              0       -2.929433    1.604423   -0.550646
   25          1              0       -3.399488   -0.453251   -1.410592
 ---------------------------------------------------------------------
```

TS5

```
-351.2579
Zero-point correction=                           0.201357
(Hartree/Particle)
 Thermal correction to Energy=                    0.215597
 Thermal correction to Enthalpy=                  0.216542
 Thermal correction to Gibbs Free Energy=         0.159911
 Sum of electronic and zero-point Energies=           -627.238710
 Sum of electronic and thermal Energies=              -627.224470
 Sum of electronic and thermal Enthalpies=            -627.223526
 Sum of electronic and thermal Free Energies=         -627.280157


---------------------------------------------------------------------
 Center     Atomic     Atomic              Coordinates (Angstroms)
 Number     Number      Type              X           Y           Z
```

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	-1.393490	0.387400	0.288813
2	6	0	-3.263491	0.915282	-0.777939
3	6	0	-3.759794	-0.505285	-0.738419
4	6	0	-3.377171	-1.158406	0.599979
5	6	0	-1.901939	-0.844505	0.942713
6	6	0	-3.145355	1.719302	0.316429
7	6	0	-0.352856	0.963992	-0.214775
8	46	0	1.440860	-0.031349	-0.072098
9	8	0	2.816559	1.653569	0.249290
10	8	0	0.576359	-1.783691	-0.392232
11	8	0	3.365195	-0.761358	0.048227
12	1	0	-2.963230	1.314007	-1.744203
13	1	0	-3.313550	-1.054389	-1.574919
14	1	0	-4.848606	-0.533332	-0.887115
15	1	0	-4.032488	-0.781692	1.394277
16	1	0	-3.538166	-2.239817	0.555690
17	1	0	-1.206472	-1.615810	0.568466
18	1	0	-1.771283	-0.772493	2.029781
19	1	0	-2.778642	2.736198	0.223799
20	1	0	-3.510643	1.429942	1.296721
21	1	0	-0.323479	1.921781	-0.721929
22	1	0	2.773416	1.865669	1.197016
23	1	0	3.444780	0.833105	0.188676
24	1	0	1.280203	-2.385517	-0.093825
25	1	0	3.608259	-1.010433	-0.859011

C9

Zero-point correction= 0.205132
(Hartree/Particle)
Thermal correction to Energy= 0.218662
Thermal correction to Enthalpy= 0.219606
Thermal correction to Gibbs Free Energy= 0.164285
Sum of electronic and zero-point Energies= -627.271584
Sum of electronic and thermal Energies= -627.258054
Sum of electronic and thermal Enthalpies= -627.257110
Sum of electronic and thermal Free Energies= -627.312431

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	-1.657008	-0.274590	-0.431485
2	6	0	-2.717414	-1.193071	0.371025
3	6	0	-3.602997	-0.217581	1.127316
4	6	0	-3.523191	1.115464	0.352081
5	6	0	-2.091906	1.174725	-0.229253
6	6	0	-2.726262	-1.205539	-1.091289
7	6	0	-0.327642	-0.751713	-0.399884
8	46	0	1.388126	0.056846	-0.061051
9	8	0	2.574425	-1.738920	0.441226
10	8	0	0.691992	1.870611	-0.398859
11	8	0	3.331095	0.610341	0.374277
12	1	0	-2.328066	-2.060224	0.895781
13	1	0	-3.211593	-0.102623	2.144871
14	1	0	-4.629743	-0.596065	1.212199
15	1	0	-4.272369	1.129220	-0.448452
16	1	0	-3.741393	1.972976	0.995582
17	1	0	-1.386433	1.653703	0.451743

18	1	0	-2.039629	1.739396	-1.164915
19	1	0	-2.347218	-2.083198	-1.605745
20	1	0	-3.499928	-0.668227	-1.632918
21	1	0	-0.272916	-1.842583	-0.528909
22	1	0	2.868271	-2.136130	-0.396324
23	1	0	3.233649	-0.952961	0.603575
24	1	0	1.530271	2.365322	-0.426851
25	1	0	3.341749	1.144028	1.184495

C10

Zero-point correction= 0.282567
(Hartree/Particle)
Thermal correction to Energy= 0.303151
Thermal correction to Enthalpy= 0.304095
Thermal correction to Gibbs Free Energy= 0.228424
Sum of electronic and zero-point Energies= -858.240410
Sum of electronic and thermal Energies= -858.219825
Sum of electronic and thermal Enthalpies= -858.218881
Sum of electronic and thermal Free Energies= -858.294553

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	46	0	2.567810	-0.577899	0.081226
2	6	0	0.521700	-0.074748	0.815651
3	6	0	0.738239	0.940065	0.157077
4	6	0	0.969312	2.243351	-0.472884
5	6	0	0.074339	3.376650	0.079471
6	6	0	-1.397537	3.338693	-0.381465
7	6	0	-2.180574	2.158404	0.120595
8	6	0	-2.828379	1.283478	-0.664752
9	8	0	3.505208	1.040173	0.652996
10	8	0	1.951015	-2.578070	-0.616859
11	8	0	4.265570	-1.594419	-0.297464
12	6	0	-3.607228	0.107043	-0.249070
13	6	0	-4.175591	-0.713801	-1.239760
14	6	0	-3.813395	-0.250758	1.097537
15	6	0	-4.916030	-1.847233	-0.905945
16	6	0	-4.551961	-1.382271	1.432595
17	6	0	-5.107411	-2.188076	0.433555
18	1	0	0.056126	-0.847953	1.390171
19	1	0	2.024625	2.480423	-0.288424
20	1	0	0.839637	2.157458	-1.560261
21	1	0	0.127233	3.372523	1.175162
22	1	0	0.515458	4.325128	-0.250744
23	1	0	-1.874478	4.265177	-0.025795
24	1	0	-1.438755	3.371174	-1.478753
25	1	0	-2.203618	2.038057	1.204140
26	1	0	-2.779781	1.436758	-1.744084
27	1	0	4.404491	0.703712	0.811264
28	1	0	1.624162	-2.504245	-1.529132
29	1	0	2.957174	-2.657083	-0.687090
30	1	0	4.654995	-1.183303	-1.087593
31	1	0	-4.031053	-0.454471	-2.286326
32	1	0	-3.397191	0.363695	1.890714
33	1	0	-5.343649	-2.463069	-1.692841
34	1	0	-4.697927	-1.636951	2.479200

35	1	0	-5.683957	-3.069934	0.698957

TS6

-346.4865
Zero-point correction= 0.282772
(Hartree/Particle)
Thermal correction to Energy= 0.301639
Thermal correction to Enthalpy= 0.302583
Thermal correction to Gibbs Free Energy= 0.234062
Sum of electronic and zero-point Energies= -858.216282
Sum of electronic and thermal Energies= -858.197414
Sum of electronic and thermal Enthalpies= -858.196470
Sum of electronic and thermal Free Energies= -858.264992

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	-0.040751	1.114466	-0.191538
2	6	0	-1.644251	1.874164	0.881327
3	6	0	-1.114884	3.294059	0.833018
4	6	0	-0.480502	3.558310	-0.540236
5	6	0	0.390451	2.340721	-0.906362
6	6	0	-2.472594	1.332146	-0.075351
7	6	0	0.320255	-0.068679	0.175124
8	46	0	2.324674	-0.542996	0.022081
9	8	0	2.908270	1.332234	0.262311
10	8	0	4.223332	-1.325985	-0.155363
11	6	0	-3.157691	0.048945	-0.011115
12	6	0	-3.903391	-0.377763	-1.129625
13	6	0	-3.110366	-0.796270	1.118137
14	6	0	-4.572541	-1.597372	-1.124500
15	6	0	-3.775374	-2.019550	1.118413
16	6	0	-4.508383	-2.425497	-0.000276
17	1	0	-1.548825	1.362755	1.834479
18	1	0	-0.360021	3.406049	1.618443
19	1	0	-1.916052	4.013076	1.049418
20	1	0	-1.263625	3.700986	-1.294884
21	1	0	0.109990	4.479791	-0.529053
22	1	0	1.442206	2.443947	-0.579370
23	1	0	0.400055	2.166882	-1.989287
24	1	0	-2.633234	1.896600	-0.992445
25	1	0	-0.306342	-0.836715	0.619265
26	1	0	3.811080	1.287667	-0.097664
27	1	0	4.606279	-1.277517	0.736510
28	1	0	-3.949268	0.260328	-2.008902
29	1	0	-2.564186	-0.491723	2.005343
30	1	0	-5.141550	-1.905319	-1.997206
31	1	0	-3.725820	-2.656840	1.996790
32	1	0	-5.028292	-3.379280	0.005711
33	8	0	2.170100	-2.722293	-0.220542
34	1	0	1.949057	-2.879648	-1.154002
35	1	0	3.190040	-2.550981	-0.212227

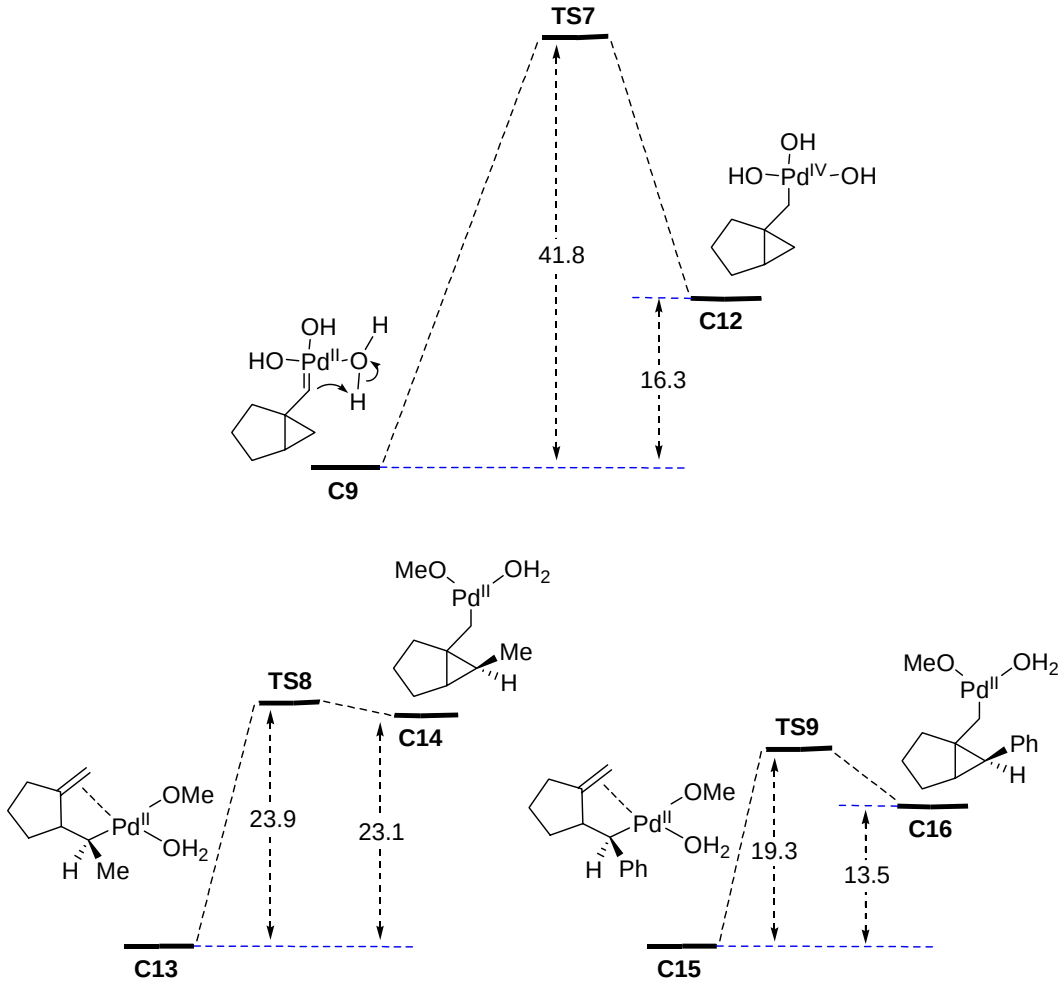
C11

```
Zero-point correction=                           0.285873
(Hartree/Particle)
 Thermal correction to Energy=                    0.304231
 Thermal correction to Enthalpy=                  0.305175
 Thermal correction to Gibbs Free Energy=         0.237275
 Sum of electronic and zero-point Energies=           -858.238085
 Sum of electronic and thermal Energies=              -858.219728
 Sum of electronic and thermal Enthalpies=            -858.218783
 Sum of electronic and thermal Free Energies=         -858.286684
```

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	0.379725	1.238603	0.117073
2	6	0	1.325387	1.745823	-1.080832
3	6	0	1.037775	3.231259	-1.225311
4	6	0	0.510995	3.696891	0.149421
5	6	0	-0.245755	2.484549	0.741803
6	6	0	1.973509	1.230044	0.124895
7	6	0	-0.290129	0.023583	-0.135490
8	46	0	-2.121254	-0.550465	0.041173
9	8	0	-2.505760	0.819589	1.408532
10	8	0	-4.014529	-1.384849	-0.023693
11	6	0	2.759413	-0.044829	0.156293
12	6	0	2.909385	-0.731447	1.372200
13	6	0	3.391960	-0.553514	-0.985096
14	6	0	3.663205	-1.900671	1.440944
15	6	0	4.148673	-1.726383	-0.917719
16	6	0	4.284793	-2.403642	0.293610
17	1	0	1.344331	1.135532	-1.978645
18	1	0	0.274853	3.364427	-2.001123
19	1	0	1.930906	3.782805	-1.545336
20	1	0	1.348987	3.991319	0.792337
21	1	0	-0.132364	4.577361	0.058868
22	1	0	-1.308624	2.494036	0.494088
23	1	0	-0.193621	2.451041	1.834450
24	1	0	2.320603	1.972162	0.842911
25	1	0	0.358900	-0.727974	-0.602642
26	1	0	-3.384036	0.515991	1.699419
27	1	0	-4.636535	-0.729787	-0.378122
28	1	0	2.420778	-0.347530	2.264552
29	1	0	3.307226	-0.025767	-1.930954
30	1	0	3.764770	-2.421685	2.388997
31	1	0	4.633387	-2.105674	-1.813207
32	1	0	4.872264	-3.316058	0.346690
33	8	0	-2.164612	-2.177542	-1.451581
34	1	0	-1.809772	-2.973952	-1.020965
35	1	0	-3.148787	-2.114033	-1.122076

1.4 Formation of Cyclopropyl Derivatives (Schemes 15 and 16)

1.4.1 From Cyclopropyl Carbenes (Scheme 15)



TS7

```
-500.2463
Zero-point correction=                           0.200249
(Hartree/Particle)
 Thermal correction to Energy=                    0.213880
 Thermal correction to Enthalpy=                  0.214824
 Thermal correction to Gibbs Free Energy=         0.158935
 Sum of electronic and zero-point Energies=           -627.204908
 Sum of electronic and thermal Energies=              -627.191277
 Sum of electronic and thermal Enthalpies=            -627.190333
 Sum of electronic and thermal Free Energies=         -627.246222

---------------------------------------------------------------------
 Center     Atomic     Atomic              Coordinates (Angstroms)
 Number     Number      Type              X           Y           Z
 ---------------------------------------------------------------------
    1         46              0        1.675912    0.013344   -0.155449
    2          8              0        1.281432   -1.933333   -0.946947
    3          6              0       -0.342923    0.040166   -1.171036
    4          6              0       -1.441745    0.175601   -0.254891
    5          6              0       -2.783757    0.806894   -0.811004
    6          6              0       -3.919344   -0.059852   -0.286746
```

7	6	0	-3.356204	-0.770098	0.965854
8	6	0	-1.851085	-0.967270	0.675766
9	6	0	-1.967453	1.574403	0.152043
10	8	0	1.503656	-0.560067	1.699249
11	8	0	2.029041	1.844170	0.389078
12	1	0	1.041615	-2.490203	-0.183929
13	1	0	-0.225095	0.960841	-1.763733
14	1	0	-2.810819	1.132385	-1.846845
15	1	0	-4.816570	0.532217	-0.065506
16	1	0	-4.193671	-0.790897	-1.057075
17	1	0	-3.870044	-1.714486	1.169706
18	1	0	-3.497422	-0.141308	1.852299
19	1	0	-1.685860	-1.914399	0.146673
20	1	0	-1.232769	-0.985535	1.579898
21	1	0	-2.311040	1.683419	1.178370
22	1	0	-1.398251	2.420187	-0.223944
23	1	0	1.790579	0.240672	2.178677
24	1	0	1.190495	2.221489	0.705215
25	1	0	0.388948	-1.373432	-1.270122

C12

Zero-point correction= 0.205205
(Hartree/Particle)
Thermal correction to Energy= 0.218984
Thermal correction to Enthalpy= 0.219928
Thermal correction to Gibbs Free Energy= 0.164211
Sum of electronic and zero-point Energies= -627.242755
Sum of electronic and thermal Energies= -627.228977
Sum of electronic and thermal Enthalpies= -627.228033
Sum of electronic and thermal Free Energies= -627.283749

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	46	0	1.629087	0.112773	-0.103326
2	8	0	2.222036	-1.550102	-0.990294
3	6	0	-0.208871	-0.175796	-1.062103
4	6	0	-1.402867	0.042708	-0.245753
5	6	0	-2.674095	0.609848	-0.956530
6	6	0	-3.869206	-0.180351	-0.444223
7	6	0	-3.399309	-0.809439	0.888090
8	6	0	-1.882386	-1.045813	0.713185
9	6	0	-1.903855	1.455071	0.007186
10	8	0	1.287774	-0.767071	1.590013
11	8	0	1.342376	1.921436	0.643085
12	1	0	2.373559	-2.199726	-0.283276
13	1	0	-0.039093	0.569447	-1.848054
14	1	0	-2.627593	0.865922	-2.011560
15	1	0	-4.760600	0.447482	-0.319966
16	1	0	-4.121137	-0.960117	-1.173934
17	1	0	-3.938346	-1.731906	1.124329
18	1	0	-3.585217	-0.118662	1.718416
19	1	0	-1.695073	-2.022637	0.249044
20	1	0	-1.326171	-1.032771	1.654884
21	1	0	-2.336391	1.678996	0.980153
22	1	0	-1.303957	2.260243	-0.410288
23	1	0	1.247291	0.016491	2.173521
24	1	0	0.430586	2.024049	0.957732

25	1	0	-0.029795	-1.195825	-1.399566

C13

```
Zero-point correction=                           0.259108
(Hartree/Particle)
 Thermal correction to Energy=                    0.274626
 Thermal correction to Enthalpy=                  0.275570
 Thermal correction to Gibbs Free Energy=         0.216142
 Sum of electronic and zero-point Energies=           -630.694772
 Sum of electronic and thermal Energies=              -630.679254
 Sum of electronic and thermal Enthalpies=            -630.678310
 Sum of electronic and thermal Free Energies=         -630.737738
```

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	2.039068	0.520616	0.387177
2	6	0	3.080529	0.160986	-0.701446
3	6	0	3.289051	-1.359487	-0.560857
4	6	0	1.871683	-1.893141	-0.260231
5	6	0	1.283092	-0.802540	0.623474
6	6	0	0.919932	1.485540	-0.026411
7	6	0	0.343472	-0.954302	1.616584
8	46	0	-0.639568	0.146726	-0.078030
9	8	0	-2.617364	-1.072842	-0.484700
10	6	0	-3.649786	-1.140404	0.495259
11	6	0	0.625481	2.651458	0.901456
12	1	0	2.545154	0.849156	1.306845
13	1	0	2.666500	0.382705	-1.693883
14	1	0	4.007825	0.733715	-0.600036
15	1	0	3.734516	-1.815356	-1.450977
16	1	0	3.954114	-1.572389	0.286314
17	1	0	1.302441	-1.993634	-1.192227
18	1	0	1.861473	-2.870777	0.233339
19	1	0	1.026647	1.822625	-1.062309
20	1	0	0.219894	-0.208885	2.398782
21	1	0	-0.118731	-1.921147	1.800181
22	1	0	-3.412646	-1.961109	1.178256
23	1	0	-3.729552	-0.209564	1.072802
24	1	0	-4.619589	-1.350504	0.024771
25	1	0	1.475627	3.353881	0.912327
26	1	0	-0.262459	3.197732	0.569895
27	1	0	0.459010	2.329956	1.936311
28	8	0	-1.916960	1.242747	-1.245998
29	1	0	-1.528515	1.322391	-2.131437
30	1	0	-2.702116	-0.209807	-1.004022

TS8

```
-59.1219
Zero-point correction=                           0.258548
(Hartree/Particle)
 Thermal correction to Energy=                    0.273317
 Thermal correction to Enthalpy=                  0.274261
```

```
 Thermal correction to Gibbs Free Energy=         0.216189
 Sum of electronic and zero-point Energies=           -630.656635
 Sum of electronic and thermal Energies=              -630.641866
 Sum of electronic and thermal Enthalpies=            -630.640922
 Sum of electronic and thermal Free Energies=         -630.698994

 ---------------------------------------------------------------------
 Center     Atomic     Atomic              Coordinates (Angstroms)
 Number     Number      Type              X           Y           Z
 ---------------------------------------------------------------------
    1          6             0        2.576599   -0.436543   -0.874289
    2          6             0        4.033997   -0.089936   -0.557684
    3          6             0        3.952860    1.120178    0.406291
    4          6             0        2.601013    0.978386    1.145542
    5          6             0        1.669052    0.265087    0.143449
    6          6             0        1.813479   -1.253775    0.130897
    7          6             0        0.369774    0.927982   -0.264042
    8         46             0       -1.223670   -0.286407    0.019825
    9          8             0       -2.557201    1.197160    0.303428
   10          6             0       -2.699870    2.184956   -0.683856
   11          6             0        0.631978   -2.110213   -0.281272
   12          1             0        2.262272   -0.493860   -1.915446
   13          1             0        4.545763   -0.938732   -0.084166
   14          1             0        4.596647    0.152227   -1.465689
   15          1             0        4.809586    1.183141    1.087223
   16          1             0        3.939239    2.044789   -0.184313
   17          1             0        2.717075    0.389426    2.065210
   18          1             0        2.197381    1.952045    1.441573
   19          1             0        2.399139   -1.677554    0.948839
   20          1             0        0.324054    1.181479   -1.331432
   21          1             0        0.165462    1.823865    0.327104
   22          1             0       -1.773113    2.758412   -0.846101
   23          1             0       -3.024297    1.786146   -1.660517
   24          1             0       -3.466759    2.899651   -0.342971
   25          1             0        0.912540   -3.119065   -0.609208
   26          1             0       -0.058643   -2.256554    0.570415
   27          1             0        0.095232   -1.672432   -1.145843
   28          8             0       -3.335315   -1.268383    0.389902
   29          1             0       -3.392193   -1.499052    1.331632
   30          1             0       -3.513715   -0.286136    0.364902
 ---------------------------------------------------------------------
```

C14

```
Zero-point correction=                           0.259134
(Hartree/Particle)
 Thermal correction to Energy=                    0.274327
 Thermal correction to Enthalpy=                  0.275271
 Thermal correction to Gibbs Free Energy=         0.215810
 Sum of electronic and zero-point Energies=           -630.657861
 Sum of electronic and thermal Energies=              -630.642669
 Sum of electronic and thermal Enthalpies=            -630.641724
 Sum of electronic and thermal Free Energies=         -630.701185

 ---------------------------------------------------------------------
 Center     Atomic     Atomic              Coordinates (Angstroms)
 Number     Number      Type              X           Y           Z
 ---------------------------------------------------------------------
    1          6             0       -2.184657   -0.451887    0.880377
    2          6             0       -3.657182   -0.107848    1.118625
```

3	6	0	-3.939830	1.090469	0.180700
4	6	0	-2.947233	0.945288	-0.996661
5	6	0	-1.717558	0.209387	-0.409841
6	6	0	-1.844455	-1.297162	-0.328265
7	6	0	-0.370478	0.871042	-0.592248
8	46	0	1.209766	-0.286754	-0.067533
9	8	0	2.586230	1.174228	-0.218550
10	6	0	2.452432	2.379328	0.487204
11	6	0	-0.591811	-2.147560	-0.312306
12	1	0	-1.515283	-0.513584	1.736686
13	1	0	-4.306179	-0.961088	0.878667
14	1	0	-3.846054	0.145319	2.167500
15	1	0	-4.985050	1.145000	-0.145475
16	1	0	-3.720319	2.021852	0.717470
17	1	0	-3.387642	0.369592	-1.821791
18	1	0	-2.663235	1.919968	-1.408019
19	1	0	-2.682874	-1.756415	-0.854568
20	1	0	-0.292529	1.797234	-0.012009
21	1	0	-0.173869	1.099014	-1.648437
22	1	0	1.595108	2.978585	0.142508
23	1	0	2.353154	2.241879	1.577440
24	1	0	3.358529	2.980249	0.306576
25	1	0	-0.783882	-3.178506	0.011231
26	1	0	-0.098387	-2.200604	-1.290385
27	1	0	0.118944	-1.797812	0.490004
28	8	0	3.294520	-1.198716	0.476575
29	1	0	3.655791	-1.624882	-0.317954
30	1	0	3.483197	-0.225558	0.347380

C15

Zero-point correction= 0.310525
(Hartree/Particle)
Thermal correction to Energy= 0.329104
Thermal correction to Enthalpy= 0.330048
Thermal correction to Gibbs Free Energy= 0.261799
Sum of electronic and zero-point Energies= -822.372512
Sum of electronic and thermal Energies= -822.353933
Sum of electronic and thermal Enthalpies= -822.352989
Sum of electronic and thermal Free Energies= -822.421238

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	0.202909	2.041165	-0.030353
2	6	0	0.976759	2.966477	-1.001456
3	6	0	2.324382	3.223468	-0.299728
4	6	0	2.676292	1.856771	0.327963
5	6	0	1.315810	1.305657	0.732082
6	6	0	-0.560983	0.884296	-0.678627
7	6	0	1.054895	0.387496	1.736715
8	6	0	-1.933272	0.531145	-0.241276
9	6	0	-4.565000	-0.212052	0.494822
10	6	0	-2.499896	0.959830	0.975218
11	6	0	-2.726525	-0.284822	-1.076389
12	6	0	-4.019868	-0.649814	-0.716177
13	6	0	-3.796983	0.594046	1.336141
14	46	0	0.742182	-0.681789	-0.138106
15	8	0	0.456556	-2.204490	-1.730850

16	8	0	2.032654	-2.381417	0.106831
17	6	0	1.928635	-3.242349	1.208323
18	1	0	-0.413917	2.651750	0.642848
19	1	0	1.152339	2.443983	-1.951067
20	1	0	0.426503	3.884245	-1.230841
21	1	0	3.099035	3.589633	-0.980912
22	1	0	2.199961	3.975122	0.490638
23	1	0	3.162371	1.208587	-0.410213
24	1	0	3.353126	1.926992	1.186532
25	1	0	-0.469466	0.882353	-1.768682
26	1	0	0.064986	0.299967	2.177904
27	1	0	1.871846	-0.051550	2.303390
28	1	0	-5.574760	-0.496281	0.777782
29	1	0	-1.928946	1.589783	1.651326
30	1	0	-2.307091	-0.639104	-2.014613
31	1	0	-4.605725	-1.278102	-1.382111
32	1	0	-4.208228	0.943115	2.280026
33	1	0	0.938117	-1.925485	-2.527028
34	1	0	1.187623	-2.627371	-1.089192
35	1	0	2.222333	-2.744907	2.148770
36	1	0	0.909308	-3.645560	1.356261
37	1	0	2.603618	-4.105505	1.080633

TS9

-54.9283
Zero-point correction= 0.311708
(Hartree/Particle)
Thermal correction to Energy= 0.329665
Thermal correction to Enthalpy= 0.330610
Thermal correction to Gibbs Free Energy= 0.264449
Sum of electronic and zero-point Energies= -822.341725
Sum of electronic and thermal Energies= -822.323767
Sum of electronic and thermal Enthalpies= -822.322823
Sum of electronic and thermal Free Energies= -822.388984

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	2.534439	0.826081	0.629492
2	6	0	3.969037	0.770460	0.086636
3	6	0	4.188987	-0.711779	-0.303349
4	6	0	2.784379	-1.256946	-0.645967
5	6	0	1.827970	-0.467437	0.267255
6	6	0	1.415671	0.970002	-0.359604
7	6	0	0.830242	-1.180750	1.099590
8	6	0	0.167857	1.746770	-0.065153
9	6	0	-2.135332	3.327258	0.356823
10	6	0	-0.280673	2.040320	1.236577
11	6	0	-0.562445	2.273632	-1.147825
12	6	0	-1.700971	3.050088	-0.940457
13	6	0	-1.419007	2.819337	1.442099
14	46	0	-0.658259	-0.907961	-0.217696
15	8	0	-2.458024	-0.914965	-1.742446
16	8	0	-1.866802	-2.500235	0.179703
17	6	0	-2.420490	-2.609893	1.464574
18	1	0	2.371298	1.257584	1.614574
19	1	0	4.084124	1.433683	-0.780200

20	1	0	4.688840	1.104706	0.840991
21	1	0	4.907840	-0.836414	-1.120433
22	1	0	4.583281	-1.256252	0.563442
23	1	0	2.549678	-1.095851	-1.705568
24	1	0	2.696034	-2.332316	-0.462649
25	1	0	1.725423	1.054795	-1.400098
26	1	0	0.563681	-0.705431	2.047886
27	1	0	1.035390	-2.244332	1.233103
28	1	0	-3.021970	3.933154	0.520648
29	1	0	0.262132	1.664152	2.098237
30	1	0	-0.226849	2.071888	-2.162376
31	1	0	-2.246587	3.440381	-1.795055
32	1	0	-1.744820	3.030515	2.457133
33	1	0	-2.143482	-1.361679	-2.545198
34	1	0	-2.641336	-1.664386	-1.099736
35	1	0	-1.654082	-2.766650	2.241521
36	1	0	-3.022403	-1.732993	1.761684
37	1	0	-3.085665	-3.489596	1.483914

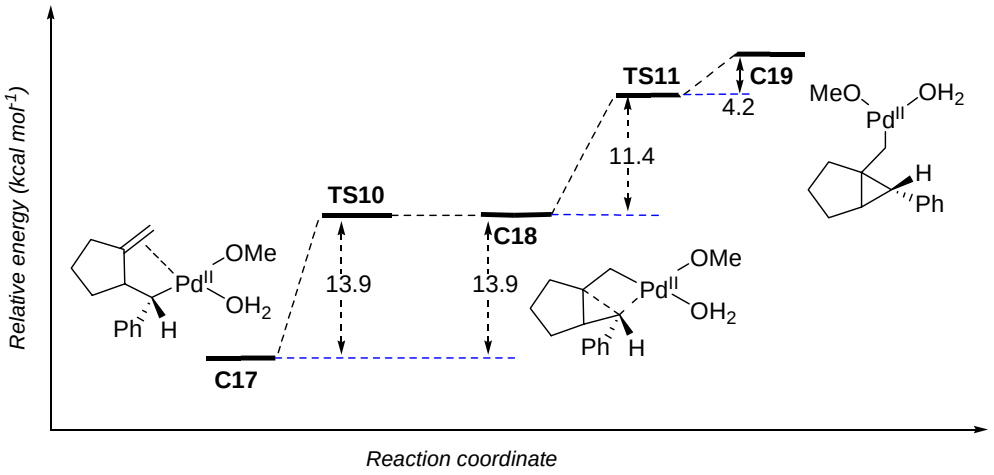
C16

Zero-point correction= 0.312337
(Hartree/Particle)
Thermal correction to Energy= 0.330731
Thermal correction to Enthalpy= 0.331675
Thermal correction to Gibbs Free Energy= 0.265441
Sum of electronic and zero-point Energies= -822.350888
Sum of electronic and thermal Energies= -822.332494
Sum of electronic and thermal Enthalpies= -822.331550
Sum of electronic and thermal Free Energies= -822.397784

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	2.632221	0.637857	0.772261
2	6	0	4.131335	0.717195	0.467635
3	6	0	4.454328	-0.607221	-0.268873
4	6	0	3.135888	-1.046411	-0.950387
5	6	0	2.011237	-0.460677	-0.072648
6	6	0	1.688384	1.008741	-0.350609
7	6	0	0.892107	-1.355678	0.423031
8	6	0	0.306078	1.532343	-0.101287
9	6	0	-2.156105	2.867219	0.376313
10	6	0	-0.359864	1.421356	1.149708
11	6	0	-0.319826	2.314884	-1.108434
12	6	0	-1.520738	2.966584	-0.874395
13	6	0	-1.577687	2.104084	1.376299
14	46	0	-0.933360	-0.581814	-0.006635
15	8	0	-3.190015	-0.294633	-0.669268
16	8	0	-1.744262	-2.398178	-0.449252
17	6	0	-1.775226	-3.397258	0.534431
18	1	0	2.297339	0.802426	1.794286
19	1	0	4.359455	1.588275	-0.161045
20	1	0	4.720887	0.825885	1.384254
21	1	0	5.288805	-0.511038	-0.972713
22	1	0	4.741399	-1.364784	0.470850
23	1	0	3.072927	-0.664415	-1.978118
24	1	0	3.057282	-2.136599	-1.013681
25	1	0	2.151054	1.438663	-1.239360

26	1	0	0.910674	-1.518156	1.508702
27	1	0	0.898865	-2.323131	-0.084028
28	1	0	-3.092930	3.386300	0.555071
29	1	0	0.139676	0.964078	1.996968
30	1	0	0.180023	2.424791	-2.067537
31	1	0	-1.966005	3.569730	-1.661397
32	1	0	-2.048641	2.027276	2.351999
33	1	0	-3.154391	-0.034639	-1.603989
34	1	0	-3.032893	-1.284849	-0.674441
35	1	0	-0.767637	-3.681471	0.881703
36	1	0	-2.367007	-3.117826	1.424506
37	1	0	-2.232908	-4.302685	0.103068

1.4.2 From Alkene Insertion into Pd-C Bond (Scheme 16)



C17

```
Zero-point correction=                           0.311343
(Hartree/Particle)
 Thermal correction to Energy=                    0.329728
 Thermal correction to Enthalpy=                  0.330672
 Thermal correction to Gibbs Free Energy=         0.263665
 Sum of electronic and zero-point Energies=           -822.365405
 Sum of electronic and thermal Energies=              -822.347020
 Sum of electronic and thermal Enthalpies=            -822.346076
 Sum of electronic and thermal Free Energies=         -822.413083
```

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	0.135539	1.908573	-0.949291
2	6	0	0.895081	2.919456	-0.050739
3	6	0	-0.199192	3.560816	0.833350
4	6	0	-1.197090	2.410416	1.097543
5	6	0	-1.207750	1.689832	-0.239315
6	6	0	0.632407	0.447282	-1.113095
7	6	0	-2.291034	1.108859	-0.875145
8	46	0	-1.000972	-0.527181	-0.217536
9	8	0	-2.419279	-1.681589	0.893409
10	6	0	-3.669482	-2.040330	0.377377

11	6	0	1.871080	-0.059195	-0.457282
12	6	0	2.870073	-0.662870	-1.245665
13	6	0	2.084783	-0.021972	0.937918
14	6	0	4.031551	-1.184435	-0.677710
15	6	0	3.246975	-0.542519	1.508084
16	6	0	4.229628	-1.123987	0.703340
17	1	0	-0.028595	2.349802	-1.940456
18	1	0	1.633635	2.412020	0.575268
19	1	0	1.439194	3.660153	-0.644869
20	1	0	0.199146	3.994993	1.756155
21	1	0	-0.705978	4.365374	0.284944
22	1	0	-0.823676	1.761863	1.899155
23	1	0	-2.196635	2.744243	1.394173
24	1	0	0.613808	0.152151	-2.165426
25	1	0	-2.291362	0.956903	-1.952882
26	1	0	-3.255840	1.044378	-0.379870
27	1	0	-4.341285	-1.170073	0.268510
28	1	0	-3.613507	-2.533529	-0.611767
29	1	0	-4.174374	-2.744365	1.060736
30	1	0	2.727758	-0.719611	-2.322205
31	1	0	1.320438	0.398522	1.585885
32	1	0	4.783250	-1.641072	-1.316481
33	1	0	3.381445	-0.497789	2.585963
34	1	0	5.133839	-1.530454	1.147865
35	8	0	-0.275822	-2.578456	0.137379
36	1	0	0.412149	-2.550051	0.823224
37	1	0	-1.203306	-2.582306	0.616219

TS10

-41.9619
Zero-point correction= 0.311465
(Hartree/Particle)
Thermal correction to Energy= 0.329291
Thermal correction to Enthalpy= 0.330235
Thermal correction to Gibbs Free Energy= 0.264954
Sum of electronic and zero-point Energies= -822.343243
Sum of electronic and thermal Energies= -822.325417
Sum of electronic and thermal Enthalpies= -822.324473
Sum of electronic and thermal Free Energies= -822.389754

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	0.947981	1.927230	-1.037061
2	6	0	2.232082	2.563346	-0.480234
3	6	0	1.881412	2.966106	0.974585
4	6	0	0.759153	1.992890	1.399101
5	6	0	-0.004536	1.722760	0.095721
6	6	0	0.693879	0.433872	-0.858125
7	6	0	-1.461431	1.807380	0.009118
8	46	0	-1.476670	-0.206606	-0.052766
9	8	0	-3.383658	-0.778995	0.434319
10	6	0	-4.470495	-0.263251	-0.284367
11	6	0	1.758106	-0.506271	-0.373415
12	6	0	2.915855	-0.673153	-1.152928
13	6	0	1.628061	-1.277050	0.791035
14	6	0	3.907858	-1.580923	-0.781912

15	6	0	2.623875	-2.179984	1.170010
16	6	0	3.767009	-2.335046	0.385096
17	1	0	0.554490	2.340683	-1.964703
18	1	0	3.070268	1.860404	-0.503372
19	1	0	2.520484	3.429254	-1.084609
20	1	0	2.746101	2.933374	1.645617
21	1	0	1.496571	3.993203	0.986469
22	1	0	1.184489	1.079994	1.824123
23	1	0	0.085563	2.416462	2.150303
24	1	0	0.115689	0.049110	-1.704387
25	1	0	-1.877790	2.205512	-0.920235
26	1	0	-1.973605	2.179274	0.896486
27	1	0	-4.581783	0.826229	-0.151900
28	1	0	-4.413956	-0.459358	-1.370807
29	1	0	-5.400074	-0.729061	0.084408
30	1	0	3.029450	-0.094943	-2.066625
31	1	0	0.731730	-1.170184	1.396544
32	1	0	4.789870	-1.699722	-1.405643
33	1	0	2.502200	-2.765431	2.077577
34	1	0	4.540266	-3.040288	0.677192
35	8	0	-1.659658	-2.512465	-0.179396
36	1	0	-1.326222	-2.914594	0.638546
37	1	0	-2.593248	-2.191777	0.043152

C18

Zero-point correction= 0.311519
(Hartree/Particle)
Thermal correction to Energy= 0.329322
Thermal correction to Enthalpy= 0.330266
Thermal correction to Gibbs Free Energy= 0.265085
Sum of electronic and zero-point Energies= -822.343190
Sum of electronic and thermal Energies= -822.325388
Sum of electronic and thermal Enthalpies= -822.324444
Sum of electronic and thermal Free Energies= -822.389625

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	0.956041	1.929551	-1.037640
2	6	0	2.239539	2.564724	-0.478892
3	6	0	1.887705	2.964966	0.976247
4	6	0	0.767234	1.989093	1.399381
5	6	0	0.004393	1.717357	0.095440
6	6	0	0.699635	0.437592	-0.855781
7	6	0	-1.453970	1.804989	0.009663
8	46	0	-1.480724	-0.207510	-0.052795
9	8	0	-3.389803	-0.770426	0.432190
10	6	0	-4.473393	-0.246721	-0.285791
11	6	0	1.761572	-0.505937	-0.372555
12	6	0	2.920070	-0.673166	-1.150715
13	6	0	1.627513	-1.279999	0.789230
14	6	0	3.909293	-1.584421	-0.780760
15	6	0	2.620410	-2.186600	1.167028
16	6	0	3.764570	-2.341864	0.383615
17	1	0	0.561682	2.343944	-1.964389
18	1	0	3.077824	1.861848	-0.502465
19	1	0	2.528374	3.431553	-1.081755
20	1	0	2.752342	2.933528	1.647453

21	1	0	1.500601	3.991219	0.988955
22	1	0	1.194056	1.076941	1.824608
23	1	0	0.092492	2.411308	2.150310
24	1	0	0.116654	0.052429	-1.698694
25	1	0	-1.868876	2.205972	-0.919238
26	1	0	-1.963535	2.181146	0.896831
27	1	0	-4.577914	0.843150	-0.151463
28	1	0	-4.418051	-0.441551	-1.372469
29	1	0	-5.405599	-0.707591	0.082507
30	1	0	3.036493	-0.092384	-2.062407
31	1	0	0.730425	-1.172766	1.393616
32	1	0	4.792147	-1.703356	-1.403269
33	1	0	2.495769	-2.774617	2.072529
34	1	0	4.535654	-3.049827	0.674876
35	8	0	-1.673008	-2.514072	-0.179459
36	1	0	-1.343149	-2.917351	0.639376
37	1	0	-2.605278	-2.189519	0.041015

TS11

-78.5354
Zero-point correction= 0.310853
(Hartree/Particle)
Thermal correction to Energy= 0.329530
Thermal correction to Enthalpy= 0.330474
Thermal correction to Gibbs Free Energy= 0.261976
Sum of electronic and zero-point Energies= -822.324524
Sum of electronic and thermal Energies= -822.305848
Sum of electronic and thermal Enthalpies= -822.304904
Sum of electronic and thermal Free Energies= -822.373402

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	0.902912	2.066043	-1.096347
2	6	0	1.920702	2.937861	-0.354890
3	6	0	1.285237	3.192481	1.032837
4	6	0	0.432548	1.936303	1.320863
5	6	0	-0.057414	1.460978	-0.060816
6	6	0	0.907296	0.571525	-0.896206
7	6	0	-1.523065	1.301535	-0.307060
8	46	0	-1.786949	-0.676159	-0.053943
9	8	0	-3.746935	-0.680492	0.181878
10	6	0	-4.535078	0.465415	0.151945
11	6	0	2.056042	-0.224752	-0.349098
12	6	0	3.286609	-0.232737	-1.023944
13	6	0	1.915874	-1.046674	0.782799
14	6	0	4.339591	-1.039890	-0.589666
15	6	0	2.968376	-1.858057	1.218754
16	6	0	4.183752	-1.857978	0.531628
17	1	0	0.498499	2.431444	-2.037414
18	1	0	2.886282	2.427883	-0.254268
19	1	0	2.105442	3.869520	-0.899883
20	1	0	2.027289	3.395702	1.813374
21	1	0	0.627319	4.068416	0.970327
22	1	0	1.033174	1.176696	1.831021
23	1	0	-0.421374	2.152900	1.970372
24	1	0	0.393620	0.045098	-1.704938

25	1	0	-1.827734	1.508277	-1.340354
26	1	0	-2.149552	1.861152	0.391674
27	1	0	-4.336333	1.166224	0.984725
28	1	0	-4.454163	1.038386	-0.790708
29	1	0	-5.587928	0.148778	0.245470
30	1	0	3.412216	0.395542	-1.902143
31	1	0	0.980417	-1.032096	1.338867
32	1	0	5.282825	-1.031137	-1.129584
33	1	0	2.838529	-2.480917	2.099929
34	1	0	5.003521	-2.485625	0.869794
35	8	0	-0.551484	-2.804400	-0.281960
36	1	0	-0.623129	-3.045206	-1.218922
37	1	0	0.397806	-2.660889	-0.120083

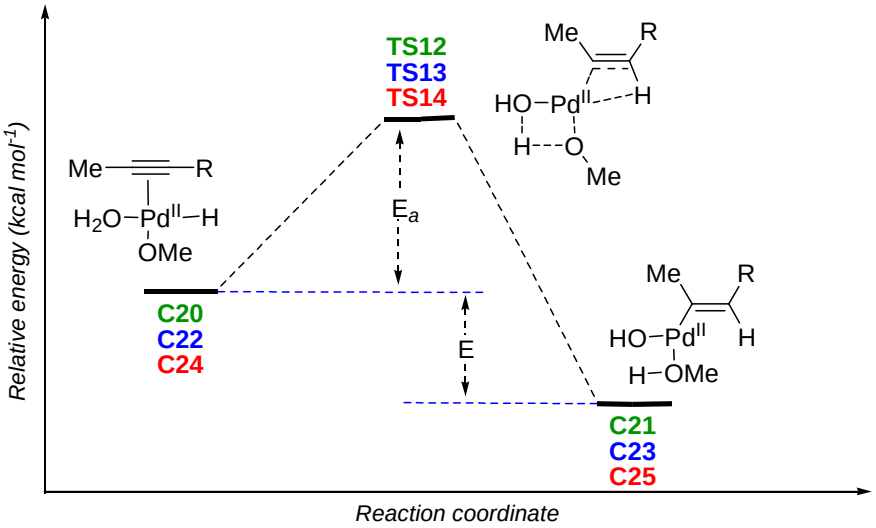
C19

Zero-point correction= 0.312533
(Hartree/Particle)
Thermal correction to Energy= 0.331305
Thermal correction to Enthalpy= 0.332249
Thermal correction to Gibbs Free Energy= 0.264193
Sum of electronic and zero-point Energies= -822.335941
Sum of electronic and thermal Energies= -822.317169
Sum of electronic and thermal Enthalpies= -822.316225
Sum of electronic and thermal Free Energies= -822.384281

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	1.041527	1.979959	-1.188039
2	6	0	1.736758	2.938114	-0.218546
3	6	0	0.808040	2.988565	1.018267
4	6	0	0.128595	1.601494	1.074137
5	6	0	0.024015	1.137213	-0.392304
6	6	0	1.237047	0.485150	-1.041352
7	6	0	-1.335411	0.821005	-0.931559
8	46	0	-2.076925	-0.873009	-0.062355
9	8	0	-3.286769	0.146994	1.091743
10	6	0	-4.448096	0.708052	0.549015
11	6	0	2.369444	-0.187481	-0.322416
12	6	0	3.697097	0.031773	-0.722109
13	6	0	2.128926	-1.125836	0.694956
14	6	0	4.749393	-0.664822	-0.127315
15	6	0	3.180789	-1.828458	1.289825
16	6	0	4.494472	-1.599929	0.879494
17	1	0	0.782331	2.344361	-2.179492
18	1	0	2.733065	2.571021	0.057788
19	1	0	1.874717	3.925251	-0.672609
20	1	0	1.339370	3.243271	1.942536
21	1	0	0.042735	3.759154	0.860246
22	1	0	0.723098	0.906503	1.676894
23	1	0	-0.869450	1.635643	1.521195
24	1	0	0.976406	-0.042528	-1.964311
25	1	0	-1.328159	0.636646	-2.014363
26	1	0	-2.073072	1.588747	-0.688270
27	1	0	-4.242336	1.492697	-0.203633
28	1	0	-5.124584	-0.028308	0.080498
29	1	0	-5.007141	1.192240	1.366943
30	1	0	3.899660	0.751882	-1.510962

31	1	0	1.112110	-1.283846	1.050378
32	1	0	5.770259	-0.479288	-0.451159
33	1	0	2.971242	-2.546707	2.078043
34	1	0	5.314491	-2.141933	1.342486
35	8	0	-0.681897	-2.264431	-1.085918
36	1	0	-0.706177	-2.092683	-2.041171
37	1	0	0.223750	-2.043001	-0.801641

2. Studies on the Alkyne Insertion into the Pd–H Bond (Scheme 28)



C20-TS12-C21 : R = H { E_a = 7.8 kcal mol^{-1} ; E = -10.7 kcal mol^{-1}

C22-TS13-C23 : R = Me { E_a = 9.6 kcal mol^{-1} ; E = -5.5 kcal mol^{-1}

C24-TS14-C25 : R = Ph { E_a = 8.8 kcal mol^{-1} ; E = -6.0 kcal mol^{-1}

2.1 Terminal Alkyne: R = H (C20-TS12-C21)

C20

Zero-point correction= 0.131980
(Hartree/Particle)
Thermal correction to Energy= 0.143952
Thermal correction to Enthalpy= 0.144896
Thermal correction to Gibbs Free Energy= 0.093249
Sum of electronic and zero-point Energies= -435.413113
Sum of electronic and thermal Energies= -435.401141
Sum of electronic and thermal Enthalpies= -435.400197
Sum of electronic and thermal Free Energies= -435.451843

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	46	0	0.049255	-0.079788	0.162571
2	6	0	-1.792157	0.412193	1.180198
3	6	0	-2.179811	-0.118040	0.131262
4	8	0	1.947193	-0.124858	-0.441388

5	8	0	0.709209	2.105066	-0.416902
6	6	0	-2.944035	-0.731804	-0.961918
7	6	0	2.925695	-1.036573	-0.016260
8	1	0	-0.026848	-1.560937	0.550783
9	1	0	-1.771712	0.906400	2.130480
10	1	0	0.446131	2.278874	-1.335074
11	1	0	1.563852	1.599439	-0.490831
12	1	0	-2.712196	-0.262862	-1.923515
13	1	0	-4.019259	-0.624737	-0.774197
14	1	0	-2.708963	-1.798301	-1.042961
15	1	0	3.882983	-0.768933	-0.491994
16	1	0	2.687581	-2.070773	-0.308936
17	1	0	3.083337	-1.024255	1.074590

TS12

-704.5074
Zero-point correction= 0.130104
(Hartree/Particle)
Thermal correction to Energy= 0.141317
Thermal correction to Enthalpy= 0.142261
Thermal correction to Gibbs Free Energy= 0.092782
Sum of electronic and zero-point Energies= -435.400733
Sum of electronic and thermal Energies= -435.389520
Sum of electronic and thermal Enthalpies= -435.388576
Sum of electronic and thermal Free Energies= -435.438055

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	46	0	-0.037048	-0.184036	-0.086862
2	6	0	1.697522	-1.524068	0.012117
3	6	0	2.051591	-0.316659	0.095395
4	8	0	-2.058198	0.085419	-0.404567
5	8	0	-0.532767	1.989385	-0.094028
6	6	0	3.033866	0.778100	0.214250
7	6	0	-3.026878	-0.446222	0.458613
8	1	0	0.080907	-1.767786	-0.099160
9	1	0	1.912301	-2.576294	-0.021635
10	1	0	-0.541755	2.301491	0.825882
11	1	0	-1.451029	1.546422	-0.238019
12	1	0	2.906293	1.497918	-0.600739
13	1	0	4.059501	0.391394	0.187211
14	1	0	2.891654	1.319350	1.156109
15	1	0	-4.023293	-0.084616	0.154897
16	1	0	-2.885485	-0.160633	1.518612
17	1	0	-3.053754	-1.546913	0.418997

C21

Zero-point correction= 0.136147
(Hartree/Particle)
Thermal correction to Energy= 0.147623
Thermal correction to Enthalpy= 0.148567
Thermal correction to Gibbs Free Energy= 0.097535
Sum of electronic and zero-point Energies= -435.430240

```
 Sum of electronic and thermal Energies=             -435.418763
 Sum of electronic and thermal Enthalpies=           -435.417819
 Sum of electronic and thermal Free Energies=        -435.468851

---------------------------------------------------------------------
 Center     Atomic     Atomic              Coordinates (Angstroms)
 Number     Number      Type              X           Y           Z
---------------------------------------------------------------------
    1         46             0       -0.028213   -0.246488   -0.092579
    2          6             0        2.406743   -1.383240   -0.026166
    3          6             0        1.910827   -0.151794    0.108295
    4          8             0       -2.312166   -0.093527   -0.420740
    5          8             0       -0.436530    1.700513   -0.395597
    6          6             0        2.650718    1.112809    0.405695
    7          6             0       -3.250699   -0.254496    0.643150
    8          1             0        1.782173   -2.236749   -0.311374
    9          1             0        3.458349   -1.619453    0.147622
   10          1             0       -0.237874    2.135051    0.450969
   11          1             0       -2.033396    0.859992   -0.480014
   12          1             0        2.447863    1.860504   -0.368785
   13          1             0        3.734050    0.938022    0.453125
   14          1             0        2.331407    1.545055    1.362251
   15          1             0       -4.200431    0.236324    0.396622
   16          1             0       -2.869102    0.149370    1.590619
   17          1             0       -3.431225   -1.325216    0.762447
---------------------------------------------------------------------
```

2.2 Internal Alkyne: R = Me (C22-TS13-C23)

C22

```
Zero-point correction=                           0.160772
(Hartree/Particle)
 Thermal correction to Energy=                    0.174447
 Thermal correction to Enthalpy=                  0.175391
 Thermal correction to Gibbs Free Energy=         0.119702
 Sum of electronic and zero-point Energies=           -474.710112
 Sum of electronic and thermal Energies=              -474.696437
 Sum of electronic and thermal Enthalpies=            -474.695493
 Sum of electronic and thermal Free Energies=         -474.751182

---------------------------------------------------------------------
 Center     Atomic     Atomic              Coordinates (Angstroms)
 Number     Number      Type              X           Y           Z
---------------------------------------------------------------------
    1         46             0       -0.201979   -0.148658   -0.087093
    2          6             0        1.850492    0.585101   -0.370362
    3          6             0        1.961099   -0.576978    0.045361
    4          8             0       -2.178983   -0.214551    0.202600
    5          6             0        2.482506   -1.891820    0.451456
    6          6             0       -3.141847   -0.381127   -0.804652
    7          6             0        2.077432    1.964125   -0.826778
    8          1             0       -0.178959   -1.064213   -1.317901
    9          1             0        2.115999   -2.180760    1.441782
   10          1             0        3.578714   -1.869398    0.482130
   11          1             0        2.170996   -2.666410   -0.257393
   12          1             0       -4.142546   -0.332141   -0.345310
   13          1             0       -3.055209   -1.357449   -1.305531
   14          1             0       -3.096711    0.399405   -1.582544
```

15	1	0	3.150188	2.193791	-0.816035
16	1	0	1.561600	2.678092	-0.176295
17	1	0	1.703971	2.105627	-1.846602
18	8	0	-0.768850	1.322790	1.664060
19	1	0	-0.656467	0.852455	2.505919
20	1	0	-1.655964	1.017548	1.320615

TS13

-624.0796
Zero-point correction= 0.158780
(Hartree/Particle)
Thermal correction to Energy= 0.171576
Thermal correction to Enthalpy= 0.172521
Thermal correction to Gibbs Free Energy= 0.119174
Sum of electronic and zero-point Energies= -474.694786
Sum of electronic and thermal Energies= -474.681990
Sum of electronic and thermal Enthalpies= -474.681046
Sum of electronic and thermal Free Energies= -474.734393

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	46	0	-0.212162	0.001089	-0.088127
2	6	0	1.894294	-0.768020	0.024867
3	6	0	1.803361	0.490636	0.103652
4	8	0	-2.225474	-0.363538	-0.406241
5	6	0	2.412353	1.832694	0.227428
6	6	0	-2.979572	-1.153384	0.472088
7	6	0	2.671522	-2.031569	-0.016192
8	1	0	0.415822	-1.457884	-0.084995
9	1	0	2.100906	2.475603	-0.602348
10	1	0	3.507627	1.770331	0.231099
11	1	0	2.091441	2.318355	1.155694
12	1	0	-4.043122	-1.110786	0.183213
13	1	0	-2.915908	-0.829973	1.529023
14	1	0	-2.676076	-2.212349	0.438198
15	1	0	3.738525	-1.792067	0.056604
16	1	0	2.499823	-2.577086	-0.950167
17	1	0	2.405447	-2.693874	0.814688
18	8	0	-1.353563	1.915718	-0.111960
19	1	0	-1.455102	2.213727	0.806960
20	1	0	-2.089389	1.206327	-0.249559

C23

Zero-point correction= 0.164523
(Hartree/Particle)
Thermal correction to Energy= 0.177722
Thermal correction to Enthalpy= 0.178666
Thermal correction to Gibbs Free Energy= 0.122136
Sum of electronic and zero-point Energies= -474.718910
Sum of electronic and thermal Energies= -474.705712
Sum of electronic and thermal Enthalpies= -474.704768
Sum of electronic and thermal Free Energies= -474.761297

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	46	0	-0.301225	-0.088426	-0.151554
2	6	0	2.188267	-0.910491	0.152893
3	6	0	1.600118	0.287510	0.079520
4	8	0	-2.592444	-0.283680	-0.456104
5	6	0	2.183277	1.662179	0.058288
6	6	0	-3.429284	-0.950245	0.487536
7	6	0	3.661672	-1.244437	0.111749
8	1	0	1.532901	-1.795433	0.236034
9	1	0	1.855453	2.215281	-0.827773
10	1	0	3.281029	1.640131	0.075015
11	1	0	1.844176	2.235400	0.929470
12	1	0	-4.467161	-0.606190	0.394566
13	1	0	-3.089069	-0.794377	1.520640
14	1	0	-3.394732	-2.018739	0.262017
15	1	0	4.275475	-0.342602	0.033980
16	1	0	3.895265	-1.887887	-0.746373
17	1	0	3.966717	-1.788833	1.015105
18	8	0	-1.109103	1.729726	0.181863
19	1	0	-0.967101	1.902012	1.127939
20	1	0	-2.488511	0.673349	-0.195150

2.3 Internal Alkyne: R = Ph (C24-TS14-C25)

C24

Zero-point correction= 0.214011
(Hartree/Particle)
Thermal correction to Energy= 0.230687
Thermal correction to Enthalpy= 0.231631
Thermal correction to Gibbs Free Energy= 0.165643
Sum of electronic and zero-point Energies= -666.391850
Sum of electronic and thermal Energies= -666.375174
Sum of electronic and thermal Enthalpies= -666.374230
Sum of electronic and thermal Free Energies= -666.440218

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	46	0	1.283293	0.124954	-0.112905
2	6	0	-0.734278	0.964757	-0.131565
3	6	0	0.051298	1.932098	-0.144538
4	8	0	2.845940	-1.090395	0.118822
5	6	0	0.631845	3.279817	-0.238000
6	6	0	3.460897	-1.861512	-0.878312
7	6	0	-1.958342	-1.197723	-0.239431
8	6	0	-1.956306	0.200890	-0.102274
9	6	0	-3.159384	-1.903558	-0.211974
10	6	0	-3.182127	0.875791	0.064345
11	6	0	-4.377396	0.162669	0.090794
12	6	0	-4.370630	-1.228318	-0.046985
13	1	0	1.431681	0.303277	-1.627904
14	1	0	1.310338	3.487018	0.596588
15	1	0	-0.164765	4.033936	-0.229057
16	1	0	1.203609	3.391340	-1.166050

17	1	0	4.277813	-2.442307	-0.420178
18	1	0	3.901585	-1.241448	-1.674232
19	1	0	2.772610	-2.578800	-1.355140
20	1	0	-1.013654	-1.716868	-0.366803
21	1	0	-3.148066	-2.984640	-0.318730
22	1	0	-3.185274	1.956322	0.172737
23	1	0	-5.316563	0.693664	0.220122
24	1	0	-5.305183	-1.782056	-0.024710
25	8	0	1.381812	-0.563340	2.135402
26	1	0	1.839219	0.117383	2.654593
27	1	0	2.109698	-1.104264	1.726240

TS14

-605.9452
Zero-point correction= 0.211820
(Hartree/Particle)
Thermal correction to Energy= 0.227713
Thermal correction to Enthalpy= 0.228658
Thermal correction to Gibbs Free Energy= 0.166205
Sum of electronic and zero-point Energies= -666.377759
Sum of electronic and thermal Energies= -666.361866
Sum of electronic and thermal Enthalpies= -666.360922
Sum of electronic and thermal Free Energies= -666.423374

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	46	0	-1.359127	0.041239	-0.077932
2	6	0	0.793724	0.608014	0.016370
3	6	0	0.008064	1.604158	0.042395
4	8	0	-2.809195	-1.413080	-0.316896
5	6	0	-0.269942	3.054716	0.070167
6	6	0	-3.001584	-2.428178	0.630805
7	6	0	2.409966	-1.297061	-0.251947
8	6	0	2.136260	0.054137	0.009373
9	6	0	3.723796	-1.761731	-0.263615
10	6	0	3.210525	0.930751	0.262907
11	6	0	4.520135	0.460069	0.248903
12	6	0	4.783045	-0.887481	-0.013961
13	1	0	-0.045647	-0.826900	0.047976
14	1	0	-0.969672	3.331138	-0.725401
15	1	0	0.651915	3.635680	-0.056438
16	1	0	-0.727973	3.342112	1.024070
17	1	0	-3.902609	-3.007355	0.368821
18	1	0	-3.142290	-2.053291	1.662504
19	1	0	-2.156163	-3.134684	0.654823
20	1	0	1.588480	-1.979861	-0.451267
21	1	0	3.918223	-2.810604	-0.468885
22	1	0	3.008126	1.976567	0.473995
23	1	0	5.338050	1.147074	0.447974
24	1	0	5.806238	-1.252280	-0.021661
25	8	0	-3.377795	0.976349	-0.217662
26	1	0	-3.648590	1.235664	0.678477
27	1	0	-3.586250	-0.030759	-0.282046

C25

```
Zero-point correction=                           0.218282
(Hartree/Particle)
 Thermal correction to Energy=                    0.234077
 Thermal correction to Enthalpy=                  0.235021
 Thermal correction to Gibbs Free Energy=         0.172675
 Sum of electronic and zero-point Energies=           -666.401330
 Sum of electronic and thermal Energies=              -666.385535
 Sum of electronic and thermal Enthalpies=            -666.384591
 Sum of electronic and thermal Free Energies=         -666.446937
```

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	46	0	-1.591596	-0.091933	-0.097122
2	6	0	1.019264	-0.242044	-0.196865
3	6	0	0.146857	0.780030	-0.158890
4	8	0	-3.732229	-0.941576	-0.138947
5	6	0	0.346108	2.259388	-0.145528
6	6	0	-4.457992	-1.262169	1.047809
7	6	0	3.217991	-1.339116	-0.567272
8	6	0	2.484522	-0.264292	-0.030356
9	6	0	4.604640	-1.394364	-0.447977
10	6	0	3.189211	0.740322	0.659283
11	6	0	4.577325	0.684424	0.776187
12	6	0	5.292620	-0.378889	0.220824
13	1	0	0.593044	-1.242721	-0.392152
14	1	0	-0.415115	2.733100	-0.774658
15	1	0	1.338747	2.540961	-0.518491
16	1	0	0.229728	2.669714	0.866997
17	1	0	-5.537531	-1.255448	0.852311
18	1	0	-4.233576	-0.564919	1.866316
19	1	0	-4.164051	-2.269528	1.351281
20	1	0	2.688837	-2.131075	-1.092501
21	1	0	5.149165	-2.231445	-0.877029
22	1	0	2.645753	1.553435	1.128462
23	1	0	5.101121	1.469909	1.314858
24	1	0	6.374033	-0.421240	0.317147
25	8	0	-2.817384	1.420158	-0.641790
26	1	0	-2.797027	2.036437	0.109802
27	1	0	-3.886056	0.013361	-0.382135

Appendix II:

X-RAY DIFFRACTION DATA

Contents ***Page***

X-ray diffraction measurements[†]

Crystal structure determination was carried out using two different diffractometers: Bruker Kappa APEX II CCD area-detector X-ray diffractometer (Mo K_α radiation, λ = 0.71073 Å).
Bruker SMART 6K CCD area-detector three-circle diffractometer with a Rigaku Rotating Anode (Cu K_α radiation, λ = 1.54178 Å) generator.

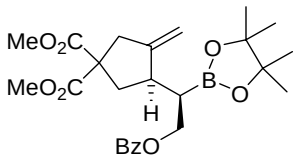
The substantial redundancy in data allows semiempirical absorption corrections (SADABS) to be applied using multiple measurements of symmetry-equivalent reflections. The raw intensity data frames were integrated with the SAINT program, which also applied corrections for Lorentz and polarization effects.

The software package SHELXTL version 6.10 was used for space group determination, structure solution and refinement. The structures was solved by direct methods or Paterson method (SHELXS-97), completed with difference Fourier syntheses, and refined with full-matrix least-squares using SHELXL-97 minimizing $\omega(F_0^2 - F_c^2)^2$. Weighted R factors (R_w) and all goodness of fit S are based on F^2; conventional R factors (R) are based on F. All non-hydrogen atoms were refined with anisotropic displacement parameters. All scattering factors and anomalous dispersions factors are contained in the SHELXTL 6.10 program library.

Single crystals suitable for X-ray diffraction were obtained by slow evaporation of a solution of the compounds in hexane at room temperature. Details of the crystal structure, data acquisition and refining are given in the corresponding tables.

[†] All the X-ray diffraction measurements were carried out at SIdI (UAM).

Dimethyl (3*R*)-3-[(1*R*)-2-(benzoyloxy)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl]-4-methylenecyclopentane-1,1-dicarboxylate (2b)



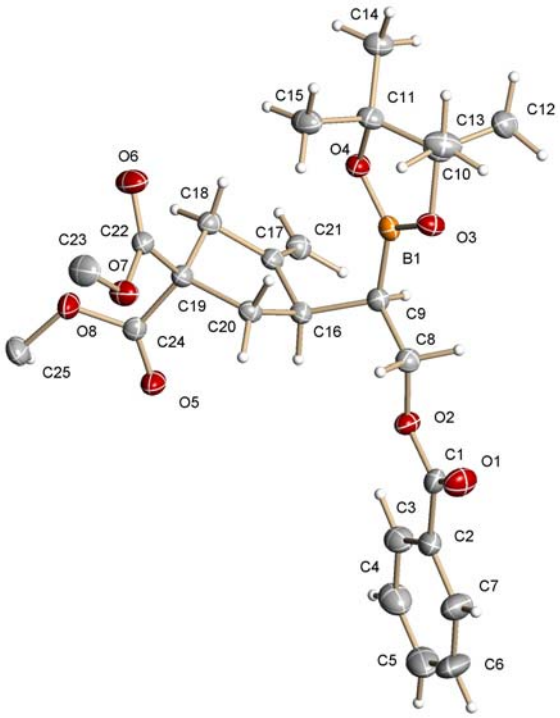


Table 1. Crystal data and structure refinement for **2b**.

Empirical formula	C25 H33 B O8	
Formula weight	472.32	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P2(1)/c	
Unit cell dimensions	a = 11.9275(3) Å	α= 90°.
	b = 6.0749(2) Å	β= 93.038(2)°.
	c = 34.4730(8) Å	γ = 90°.
Volume	2494.35(12) $Å^3$	
Z	4	
Density (calculated)	1.258 Mg/m^3	
Absorption coefficient	0.761 mm^{-1}	
F(000)	1008	
Crystal size	0.10 x 0.08 x 0.04 mm^3	
Theta range for data collection	2.57 to 67.70°.	
Index ranges	-12<=h<=14, -6<=k<=6, -40<=l<=37	
Reflections collected	13510	
Independent reflections	4403 [R(int) = 0.0675]	

Completeness to theta = 67.70°	97.4 %
Absorption correction	Semi-empirical from equivalents
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4403 / 0 / 439
Goodness-of-fit on F^2	0.983
Final R indices [I>2sigma(I)]	R1 = 0.0444, wR2 = 0.0997
R indices (all data)	R1 = 0.0748, wR2 = 0.1146
Largest diff. peak and hole	0.239 and -0.227 e.Å^{-3}

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for **2b**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	-373(2)	-585(4)	1282(1)	25(1)
C(2)	-845(2)	-1401(4)	1649(1)	29(1)
C(3)	-620(2)	-370(4)	2003(1)	33(1)
C(4)	-1074(2)	-1198(5)	2335(1)	44(1)
C(5)	-1755(2)	-3047(6)	2311(1)	52(1)
C(6)	-1976(2)	-4073(6)	1958(1)	59(1)
C(7)	-1522(2)	-3257(5)	1627(1)	44(1)
C(8)	780(2)	2074(4)	1000(1)	24(1)
C(9)	1416(2)	4141(4)	1115(1)	22(1)
C(10)	1876(2)	6323(4)	102(1)	27(1)
C(11)	2909(2)	7305(4)	340(1)	24(1)
C(12)	938(2)	7979(4)	31(1)	31(1)
C(13)	2131(3)	5146(4)	-272(1)	36(1)
C(14)	3128(2)	9717(4)	269(1)	28(1)
C(15)	3985(2)	6005(4)	296(1)	33(1)
C(16)	2370(2)	3689(4)	1426(1)	20(1)
C(17)	2911(2)	5773(3)	1596(1)	22(1)
C(18)	4153(2)	5743(4)	1521(1)	23(1)
C(19)	4433(2)	3292(4)	1473(1)	21(1)
C(20)	3343(2)	2344(4)	1271(1)	20(1)
C(21)	2369(2)	7314(4)	1782(1)	25(1)
C(22)	5427(2)	2852(4)	1222(1)	22(1)
C(23)	6497(2)	-25(5)	964(1)	37(1)
C(24)	4673(2)	2271(3)	1871(1)	21(1)
C(25)	6103(2)	1575(5)	2358(1)	32(1)
B(1)	1831(2)	5330(4)	740(1)	22(1)
O(1)	-531(1)	-1448(3)	968(1)	37(1)
O(2)	257(1)	1219(2)	1341(1)	25(1)
O(3)	1469(1)	4691(2)	375(1)	26(1)

O(4)	2591(1)	7022(2)	741(1)	24(1)
O(5)	3986(1)	1498(3)	2074(1)	28(1)
O(6)	5980(1)	4205(3)	1069(1)	34(1)
O(7)	5571(1)	678(3)	1186(1)	28(1)
O(8)	5762(1)	2451(3)	1980(1)	29(1)

Table 3. Bond lengths [Å] and angles [°]for **2b**.

C(1)-O(2)	1.339(3)	C(15)-H(15B)	0.97(3)
C(1)-C(2)	1.494(3)	C(15)-H(15A)	0.98(3)
C(2)-C(3)	1.386(4)	C(16)-C(17)	1.524(3)
C(2)-C(7)	1.387(4)	C(16)-C(20)	1.538(3)
C(3)-C(4)	1.388(4)	C(16)-H(16)	0.98(2)
C(3)-H(3)	0.98(3)	C(17)-C(21)	1.322(3)
C(4)-C(5)	1.386(5)	C(17)-C(18)	1.518(3)
C(4)-H(4)	0.96(4)	C(18)-C(19)	1.537(3)
C(5)-C(6)	1.380(5)	C(18)-H(18B)	0.94(2)
C(5)-H(5)	0.99(3)	C(18)-H(18A)	0.96(3)
C(6)-C(7)	1.382(4)	C(19)-C(24)	1.521(3)
C(6)-H(6)	0.92(4)	C(19)-C(22)	1.529(3)
C(7)-H(7)	0.96(3)	C(19)-C(20)	1.551(3)
C(8)-O(2)	1.456(2)	C(20)-H(20B)	0.97(2)
C(8)-C(9)	1.509(3)	C(20)-H(20A)	0.97(3)
C(8)-H(8A)	0.98(2)	C(21)-H(21B)	0.96(3)
C(8)-H(8B)	1.02(2)	C(21)-H(21A)	1.01(3)
C(9)-C(16)	1.547(3)	C(22)-O(6)	1.193(3)
C(9)-B(1)	1.583(3)	C(22)-O(7)	1.338(3)
C(9)-H(9A)	1.00(2)	C(23)-O(7)	1.442(3)
C(10)-O(3)	1.466(3)	C(24)-O(5)	1.200(3)
C(10)-C(12)	1.515(3)	C(24)-O(8)	1.337(2)
C(10)-C(13)	1.521(3)	C(25)-O(8)	1.448(3)
C(10)-C(11)	1.562(3)	B(1)-O(3)	1.367(3)
C(11)-O(4)	1.462(2)	B(1)-O(4)	1.371(3)
C(11)-C(14)	1.511(3)	O(1)-C(1)-O(2)	123.4(2)
C(11)-C(15)	1.522(3)	O(1)-C(1)-C(2)	124.5(2)
C(12)-H(12B)	0.98(3)	O(2)-C(1)-C(2)	112.11(19)
C(12)-H(12A)	0.95(3)	C(3)-C(2)-C(1)	122.1(2)
C(12)-H(12C)	1.00(3)	C(7)-C(2)-C(1)	117.9(2)
C(13)-H(13A)	1.01(3)	O(2)-C(8)-C(9)	108.36(17)
C(13)-H(13B)	0.97(3)	O(2)-C(8)-H(8A)	106.2(14)
C(13)-H(13C)	0.96(3)	C(9)-C(8)-H(8A)	112.8(13)
C(14)-H(14A)	0.98(2)	O(2)-C(8)-H(8B)	106.8(13)
C(14)-H(14C)	0.99(3)	C(9)-C(8)-H(8B)	109.7(13)
C(14)-H(14B)	0.94(3)	H(8A)-C(8)-H(8B)	112.7(19)
C(15)-H(15C)	0.97(3)	C(8)-C(9)-C(16)	112.05(18)

C(8)-C(9)-B(1)	109.82(18)	C(17)-C(18)-H(18A)	111.9(14)
C(16)-C(9)-B(1)	113.39(17)	C(19)-C(18)-H(18A)	114.1(15)
C(8)-C(9)-H(9A)	108.4(13)	H(18B)-C(18)-H(18A)	108(2)
C(16)-C(9)-H(9A)	106.5(13)	C(24)-C(19)-C(22)	108.97(17)
B(1)-C(9)-H(9A)	106.3(14)	C(24)-C(19)-C(18)	109.20(17)
O(3)-C(10)-C(12)	106.66(17)	C(22)-C(19)-C(18)	114.21(17)
O(3)-C(10)-C(13)	108.30(18)	C(24)-C(19)-C(20)	111.50(17)
C(12)-C(10)-C(13)	110.7(2)	C(22)-C(19)-C(20)	109.79(17)
O(3)-C(10)-C(11)	101.54(16)	C(16)-C(20)-C(19)	106.10(17)
C(12)-C(10)-C(11)	112.77(19)	C(16)-C(20)-H(20B)	109.4(13)
C(13)-C(10)-C(11)	116.0(2)	C(19)-C(20)-H(20B)	106.2(13)
O(4)-C(11)-C(14)	108.86(17)	C(16)-C(20)-H(20A)	114.2(14)
O(4)-C(11)-C(15)	107.22(17)	C(19)-C(20)-H(20A)	114.0(14)
C(14)-C(11)-C(15)	109.46(19)	H(20B)-C(20)-H(20A)	106.6(19)
O(4)-C(11)-C(10)	102.42(16)	C(17)-C(21)-H(21B)	122.9(14)
C(14)-C(11)-C(10)	115.04(19)	C(17)-C(21)-H(21A)	120.9(14)
C(15)-C(11)-C(10)	113.27(19)	H(21B)-C(21)-H(21A)	116(2)
C(17)-C(16)-C(20)	105.23(16)	O(6)-C(22)-O(7)	124.33(19)
C(17)-C(16)-C(9)	113.58(17)	O(6)-C(22)-C(19)	126.3(2)
C(20)-C(16)-C(9)	113.26(17)	O(7)-C(22)-C(19)	109.34(17)
C(17)-C(16)-H(16)	107.1(14)	O(5)-C(24)-O(8)	123.6(2)
C(20)-C(16)-H(16)	109.2(13)	O(5)-C(24)-C(19)	125.65(19)
C(9)-C(16)-H(16)	108.2(13)	O(8)-C(24)-C(19)	110.69(17)
C(21)-C(17)-C(18)	126.8(2)	O(3)-B(1)-O(4)	113.06(19)
C(21)-C(17)-C(16)	124.49(19)	O(3)-B(1)-C(9)	121.8(2)
C(18)-C(17)-C(16)	108.75(17)	O(4)-B(1)-C(9)	125.13(19)
C(17)-C(18)-C(19)	104.45(17)	C(1)-O(2)-C(8)	115.49(16)
C(17)-C(18)-H(18B)	111.2(12)	B(1)-O(3)-C(10)	107.45(17)
C(19)-C(18)-H(18B)	107.2(13)	B(1)-O(4)-C(11)	106.88(16)

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for **2b**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	19(1)	25(1)	32(1)	1(1)	-2(1)	-1(1)
C(2)	21(1)	30(1)	35(1)	8(1)	2(1)	1(1)
C(3)	30(1)	34(2)	35(1)	5(1)	10(1)	1(1)
C(4)	42(2)	52(2)	38(2)	11(1)	12(1)	7(1)
C(5)	36(1)	70(2)	50(2)	28(2)	14(1)	0(1)
C(6)	41(2)	63(2)	71(2)	31(2)	-1(2)	-26(2)
C(7)	40(1)	47(2)	46(2)	12(1)	-4(1)	-16(1)
C(8)	25(1)	27(1)	20(1)	2(1)	2(1)	-2(1)
C(9)	21(1)	21(1)	24(1)	1(1)	1(1)	1(1)
C(10)	37(1)	24(1)	20(1)	2(1)	1(1)	-2(1)

C(11)	30(1)	22(1)	21(1)	3(1)	5(1)	1(1)
C(12)	32(1)	33(2)	27(1)	4(1)	-3(1)	-1(1)
C(13)	58(2)	28(2)	23(1)	-1(1)	10(1)	-4(1)
C(14)	35(1)	23(1)	25(1)	0(1)	7(1)	-2(1)
C(15)	32(1)	29(2)	40(2)	7(1)	12(1)	4(1)
C(16)	21(1)	21(1)	19(1)	2(1)	1(1)	0(1)
C(17)	23(1)	24(1)	19(1)	5(1)	-1(1)	-2(1)
C(18)	24(1)	24(1)	21(1)	2(1)	0(1)	-3(1)
C(19)	21(1)	22(1)	21(1)	2(1)	0(1)	-2(1)
C(20)	24(1)	18(1)	19(1)	0(1)	0(1)	-1(1)
C(21)	27(1)	26(1)	22(1)	1(1)	0(1)	-1(1)
C(22)	21(1)	23(1)	22(1)	2(1)	0(1)	-1(1)
C(23)	33(1)	35(2)	43(2)	0(1)	14(1)	9(1)
C(24)	22(1)	18(1)	24(1)	-3(1)	0(1)	-1(1)
C(25)	29(1)	40(2)	26(1)	9(1)	-4(1)	1(1)
B(1)	21(1)	21(1)	24(1)	0(1)	0(1)	4(1)
O(1)	43(1)	35(1)	32(1)	-6(1)	-1(1)	-13(1)
O(2)	25(1)	27(1)	23(1)	2(1)	2(1)	-6(1)
O(3)	33(1)	23(1)	20(1)	2(1)	1(1)	-4(1)
O(4)	24(1)	26(1)	21(1)	3(1)	2(1)	-2(1)
O(5)	24(1)	36(1)	24(1)	7(1)	1(1)	-5(1)
O(6)	32(1)	28(1)	43(1)	6(1)	14(1)	-1(1)
O(7)	29(1)	24(1)	33(1)	1(1)	10(1)	3(1)
O(8)	22(1)	40(1)	25(1)	8(1)	-4(1)	-5(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3) for **2b**.

	x	y	z	U(eq)
H(18B)	4292(16)	6440(40)	1286(6)	13(5)
H(14A)	2481(19)	10640(40)	328(7)	21(6)
H(15C)	3875(19)	4430(50)	324(7)	26(6)
H(16)	2051(18)	2890(40)	1642(7)	21(6)
H(13A)	2680(20)	3900(50)	-223(8)	39(7)
H(14C)	3310(20)	9920(40)	-5(8)	31(7)
H(20B)	3393(17)	2630(40)	995(7)	16(5)
H(8A)	1270(19)	900(40)	912(7)	21(6)
H(9A)	885(19)	5180(40)	1235(7)	24(6)
H(18A)	4600(20)	6470(40)	1724(8)	29(6)
H(13B)	2430(20)	6170(50)	-457(8)	39(7)
H(21B)	2733(19)	8610(40)	1890(7)	25(6)
H(20A)	3263(19)	760(40)	1300(7)	26(6)
H(25A)	5700(20)	2290(40)	2563(8)	31(7)
H(12B)	270(20)	7140(40)	-62(8)	35(7)

H(5)	-2060(20)	-3570(50)	2556(9)	50(8)
H(12A)	1130(19)	9030(40)	-159(7)	25(6)
H(21A)	1530(20)	7220(40)	1806(7)	30(6)
H(12C)	750(20)	8730(40)	278(8)	33(7)
H(14B)	3760(20)	10280(50)	414(8)	37(7)
H(3)	-140(20)	940(50)	2010(7)	33(7)
H(8B)	150(20)	2440(40)	802(7)	23(6)
H(23B)	7190(20)	560(40)	1087(7)	27(6)
H(4)	-910(30)	-460(60)	2578(11)	68(11)
H(23A)	6500(20)	-1660(60)	976(8)	46(8)
H(13C)	1460(20)	4460(50)	-382(9)	48(8)
H(25B)	5940(20)	0(60)	2356(8)	44(8)
H(25C)	6920(30)	1710(50)	2380(9)	52(9)
H(15B)	4540(20)	6630(50)	480(8)	42(8)
H(15A)	4230(20)	6240(50)	31(8)	37(7)
H(23C)	6380(20)	460(50)	694(9)	48(8)
H(6)	-2420(30)	-5310(60)	1936(10)	65(10)
H(7)	-1660(30)	-4060(50)	1388(10)	54(9)

Tetramethyl (1'*S*,5'*E*)-5'-ethylidene-5-[(1*R*)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl]-1,1'-bi(cyclopentan)-5-ene-3,3,3',3'-tetracarboxylate (26b)

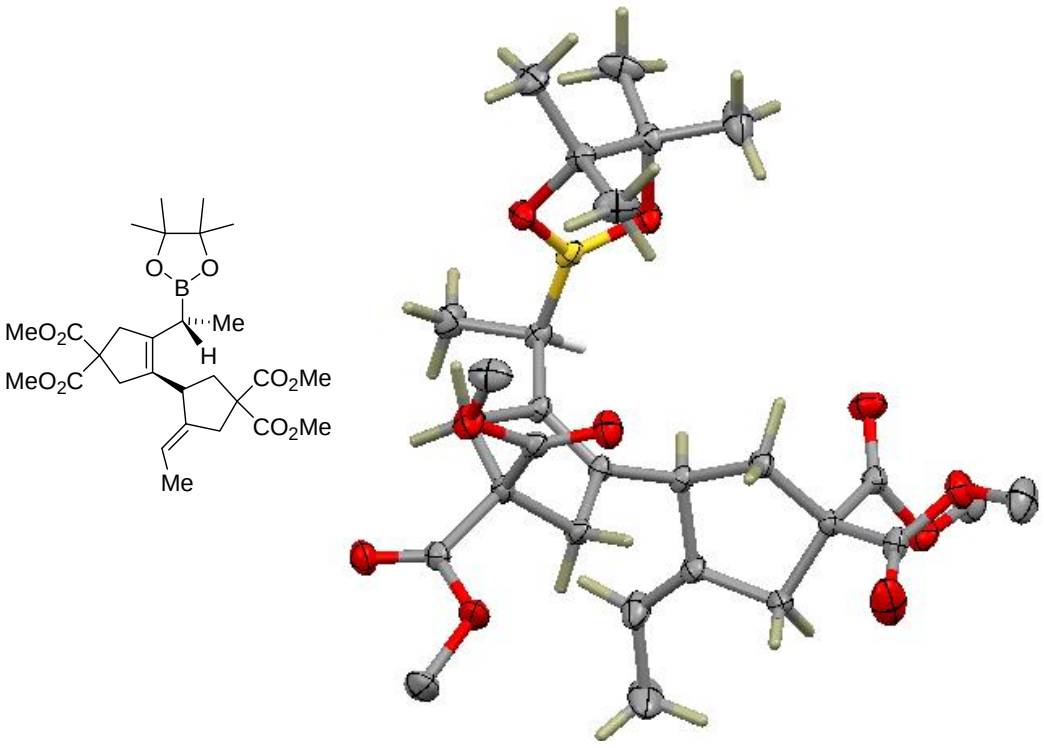


Table 1. Crystal data and structure refinement for **26b**.

Empirical formula	C28 H41 B O10	
Formula weight	548.42	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)/n	
Unit cell dimensions	a = 23.1455(14) Å	α= 90°.
	b = 14.6173(8) Å	β= 106.200(4)°.
	c = 27.1871(16) Å	γ = 90°.
Volume	8832.8(9) $Å^3$	
Z	12	
Density (calculated)	1.237 Mg/m^3	
Absorption coefficient	0.092 mm^{-1}	
F(000)	3528	
Crystal size	0.35 x 0.25 x 0.10 mm^3	
Theta range for data collection	1.02 to 32.04°.	
Index ranges	-34<=h<=33, -21<=k<=21, -40<=l<=40	
Reflections collected	162974	
Independent reflections	30426 [R(int) = 0.0528]	
Completeness to theta = 32.04°	98.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9908 and 0.9684	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	30426 / 0 / 1084	
Goodness-of-fit on F^2	1.032	
Final R indices [I>2sigma(I)]	R1 = 0.0503, wR2 = 0.1297	
R indices (all data)	R1 = 0.0866, wR2 = 0.1662	
Largest diff. peak and hole	0.744 and -0.364 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **26b**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
B(1)	4642(1)	9900(1)	1867(1)	17(1)
B(2)	1361(1)	10106(1)	8580(1)	18(1)
B(3)	6980(1)	5186(1)	9799(1)	17(1)

C(1)	4824(1)	8688(1)	1409(1)	19(1)
C(2)	4208(1)	8569(1)	1522(1)	20(1)
C(3)	5328(1)	8156(1)	1775(1)	31(1)
C(4)	4818(1)	8500(1)	860(1)	29(1)
C(5)	4098(1)	7635(1)	1718(1)	35(1)
C(6)	3681(1)	8847(1)	1071(1)	32(1)
C(7)	4755(1)	10818(1)	2184(1)	18(1)
C(8)	4705(1)	11663(1)	1837(1)	26(1)
C(9)	5364(1)	10740(1)	2570(1)	16(1)
C(10)	5485(1)	10511(1)	3066(1)	16(1)
C(11)	6153(1)	10498(1)	3324(1)	18(1)
C(12)	6439(1)	10544(1)	2874(1)	17(1)
C(13)	5933(1)	10896(1)	2411(1)	18(1)
C(14)	6626(1)	9589(1)	2748(1)	19(1)
C(15)	7152(1)	8784(1)	2255(1)	31(1)
C(16)	6995(1)	11152(1)	3009(1)	19(1)
C(17)	7935(1)	11349(1)	3635(1)	32(1)
C(18)	5053(1)	10283(1)	3370(1)	16(1)
C(19)	5099(1)	9272(1)	3544(1)	18(1)
C(20)	4945(1)	9277(1)	4062(1)	16(1)
C(21)	5222(1)	10177(1)	4311(1)	20(1)
C(22)	5171(1)	10828(1)	3868(1)	18(1)
C(23)	5224(1)	11730(1)	3899(1)	29(1)
C(24)	5335(1)	12285(1)	4380(1)	44(1)
C(25)	5232(1)	8448(1)	4377(1)	22(1)
C(26)	5112(1)	6890(1)	4550(1)	35(1)
C(27)	4266(1)	9250(1)	3975(1)	18(1)
C(28)	3497(1)	9403(1)	4386(1)	29(1)
C(29)	874(1)	8830(1)	8199(1)	20(1)
C(30)	1498(1)	8910(1)	8091(1)	21(1)
C(31)	359(1)	9160(1)	7755(1)	28(1)
C(32)	732(1)	7898(1)	8380(1)	33(1)
C(33)	1493(1)	8753(1)	7539(1)	31(1)
C(34)	1981(1)	8324(1)	8449(1)	34(1)
C(35)	1521(1)	10990(1)	8923(1)	18(1)
C(36)	1521(1)	11864(1)	8607(1)	27(1)
C(37)	2125(1)	10819(1)	9303(1)	16(1)
C(38)	2234(1)	10545(1)	9792(1)	15(1)
C(39)	2897(1)	10411(1)	10044(1)	17(1)
C(40)	3186(1)	10471(1)	9596(1)	16(1)
C(41)	2701(1)	10915(1)	9148(1)	19(1)
C(42)	3329(1)	9513(1)	9436(1)	18(1)
C(43)	3816(1)	8695(1)	8920(1)	28(1)
C(44)	3770(1)	11008(1)	9753(1)	19(1)
C(45)	4730(1)	11017(1)	10368(1)	29(1)
C(46)	1789(1)	10363(1)	10090(1)	16(1)

C(47)	1730(1)	9330(1)	10193(1)	17(1)
C(48)	1608(1)	9284(1)	10722(1)	15(1)
C(49)	2006(1)	10057(1)	11021(1)	18(1)
C(50)	1966(1)	10794(1)	10624(1)	18(1)
C(51)	2050(1)	11682(1)	10714(1)	32(1)
C(52)	2203(1)	12133(1)	11230(1)	48(1)
C(53)	955(1)	9519(1)	10676(1)	18(1)
C(54)	233(1)	9638(1)	11139(1)	30(1)
C(55)	1772(1)	8349(1)	10966(1)	18(1)
C(56)	1457(1)	6801(1)	10917(1)	28(1)
C(57)	6805(1)	3980(1)	10266(1)	18(1)
C(58)	7429(1)	3871(1)	10161(1)	18(1)
C(59)	6311(1)	3424(1)	9902(1)	29(1)
C(60)	6804(1)	3814(1)	10816(1)	27(1)
C(61)	7947(1)	4166(1)	10615(1)	27(1)
C(62)	7552(1)	2940(1)	9970(1)	29(1)
C(63)	6857(1)	6096(1)	9475(1)	19(1)
C(64)	6865(1)	6945(1)	9813(1)	28(1)
C(65)	6261(1)	5981(1)	9074(1)	17(1)
C(66)	6164(1)	5722(1)	8584(1)	16(1)
C(67)	5502(1)	5639(1)	8311(1)	19(1)
C(68)	5194(1)	5705(1)	8747(1)	18(1)
C(69)	5674(1)	6124(1)	9207(1)	20(1)
C(70)	5026(1)	4753(1)	8897(1)	18(1)
C(71)	4491(1)	3970(1)	9392(1)	28(1)
C(72)	4618(1)	6263(1)	8578(1)	21(1)
C(73)	3669(1)	6302(1)	7951(1)	35(1)
C(74)	6621(1)	5506(1)	8302(1)	16(1)
C(75)	6642(1)	4473(1)	8187(1)	18(1)
C(76)	6805(1)	4425(1)	7675(1)	15(1)
C(77)	6459(1)	5235(1)	7371(1)	18(1)
C(78)	6484(1)	5960(1)	7773(1)	16(1)
C(79)	6405(1)	6850(1)	7687(1)	24(1)
C(80)	6280(1)	7304(1)	7172(1)	30(1)
C(81)	7481(1)	4527(1)	7766(1)	17(1)
C(82)	8237(1)	4661(1)	7337(1)	30(1)
C(83)	6608(1)	3508(1)	7414(1)	19(1)
C(84)	6899(1)	1950(1)	7425(1)	30(1)
O(1)	4951(1)	9661(1)	1524(1)	20(1)
O(2)	4241(1)	9252(1)	1924(1)	20(1)
O(3)	6472(1)	8883(1)	2898(1)	28(1)
O(4)	6971(1)	9644(1)	2427(1)	25(1)
O(5)	7070(1)	11836(1)	2791(1)	26(1)
O(6)	7394(1)	10819(1)	3430(1)	26(1)
O(7)	5739(1)	8430(1)	4650(1)	41(1)
O(8)	4864(1)	7734(1)	4294(1)	27(1)

O(9)	3903(1)	9093(1)	3574(1)	29(1)
O(10)	4128(1)	9423(1)	4414(1)	22(1)
O(11)	931(1)	9491(1)	8616(1)	21(1)
O(12)	1658(1)	9864(1)	8227(1)	22(1)
O(13)	3160(1)	8807(1)	9576(1)	27(1)
O(14)	3659(1)	9562(1)	9104(1)	24(1)
O(15)	3876(1)	11719(1)	9575(1)	28(1)
O(16)	4159(1)	10575(1)	10146(1)	25(1)
O(17)	617(1)	9865(1)	10310(1)	36(1)
O(18)	819(1)	9344(1)	11114(1)	23(1)
O(19)	2221(1)	8174(1)	11298(1)	34(1)
O(20)	1354(1)	7736(1)	10737(1)	23(1)
O(21)	6668(1)	4947(1)	10141(1)	19(1)
O(22)	7394(1)	4549(1)	9756(1)	20(1)
O(23)	5190(1)	4040(1)	8763(1)	26(1)
O(24)	4675(1)	4823(1)	9213(1)	24(1)
O(25)	4516(1)	6973(1)	8758(1)	30(1)
O(26)	4236(1)	5848(1)	8177(1)	29(1)
O(27)	7851(1)	4543(1)	8176(1)	28(1)
O(28)	7609(1)	4596(1)	7314(1)	22(1)
O(29)	6135(1)	3365(1)	7106(1)	35(1)
O(30)	7031(1)	2881(1)	7600(1)	23(1)

Table 3. Bond lengths [Å] and angles [°] for **26b**.

B(1)-O(2)	1.3648(16)	C(4)-H(4B)	0.9800
B(1)-O(1)	1.3703(15)	C(4)-H(4C)	0.9800
B(1)-C(7)	1.5759(18)	C(5)-H(5A)	0.9800
B(2)-O(11)	1.3656(17)	C(5)-H(5B)	0.9800
B(2)-O(12)	1.3736(16)	C(5)-H(5C)	0.9800
B(2)-C(35)	1.5750(18)	C(6)-H(6A)	0.9800
B(3)-O(22)	1.3651(16)	C(6)-H(6B)	0.9800
B(3)-O(21)	1.3732(15)	C(6)-H(6C)	0.9800
B(3)-C(63)	1.5774(18)	C(7)-C(9)	1.5083(17)
C(1)-O(1)	1.4674(15)	C(7)-C(8)	1.5382(17)
C(1)-C(4)	1.5149(17)	C(7)-H(7)	1.0000
C(1)-C(3)	1.5205(19)	C(8)-H(8A)	0.9800
C(1)-C(2)	1.5490(17)	C(8)-H(8B)	0.9800
C(2)-O(2)	1.4662(15)	C(8)-H(8C)	0.9800
C(2)-C(5)	1.5121(19)	C(9)-C(10)	1.3404(16)
C(2)-C(6)	1.523(2)	C(9)-C(13)	1.5127(16)
C(3)-H(3A)	0.9800	C(10)-C(18)	1.5019(16)
C(3)-H(3B)	0.9800	C(10)-C(11)	1.5100(17)
C(3)-H(3C)	0.9800	C(11)-C(12)	1.5474(16)
C(4)-H(4A)	0.9800	C(11)-H(11A)	0.9900

C(11)-H(11B)	0.9900	C(28)-H(28B)	0.9800
C(12)-C(16)	1.5222(17)	C(28)-H(28C)	0.9800
C(12)-C(14)	1.5277(17)	C(29)-O(11)	1.4679(14)
C(12)-C(13)	1.5495(17)	C(29)-C(32)	1.5142(19)
C(13)-H(13A)	0.9900	C(29)-C(31)	1.5213(19)
C(13)-H(13B)	0.9900	C(29)-C(30)	1.5556(18)
C(14)-O(3)	1.2000(15)	C(30)-O(12)	1.4648(15)
C(14)-O(4)	1.3408(15)	C(30)-C(33)	1.5160(18)
C(15)-O(4)	1.4428(16)	C(30)-C(34)	1.524(2)
C(15)-H(15A)	0.9800	C(31)-H(31A)	0.9800
C(15)-H(15B)	0.9800	C(31)-H(31B)	0.9800
C(15)-H(15C)	0.9800	C(31)-H(31C)	0.9800
C(16)-O(5)	1.1998(15)	C(32)-H(32A)	0.9800
C(16)-O(6)	1.3444(16)	C(32)-H(32B)	0.9800
C(17)-O(6)	1.4452(16)	C(32)-H(32C)	0.9800
C(17)-H(17A)	0.9800	C(33)-H(33A)	0.9800
C(17)-H(17B)	0.9800	C(33)-H(33B)	0.9800
C(17)-H(17C)	0.9800	C(33)-H(33C)	0.9800
C(18)-C(22)	1.5288(16)	C(34)-H(34A)	0.9800
C(18)-C(19)	1.5467(16)	C(34)-H(34B)	0.9800
C(18)-H(18)	1.0000	C(34)-H(34C)	0.9800
C(19)-C(20)	1.5456(16)	C(35)-C(37)	1.5106(17)
C(19)-H(19A)	0.9900	C(35)-C(36)	1.5410(17)
C(19)-H(19B)	0.9900	C(35)-H(35)	1.0000
C(20)-C(27)	1.5229(17)	C(36)-H(36A)	0.9800
C(20)-C(25)	1.5249(17)	C(36)-H(36B)	0.9800
C(20)-C(21)	1.5353(16)	C(36)-H(36C)	0.9800
C(21)-C(22)	1.5125(17)	C(37)-C(38)	1.3419(16)
C(21)-H(21A)	0.9900	C(37)-C(41)	1.5137(16)
C(21)-H(21B)	0.9900	C(38)-C(46)	1.4997(16)
C(22)-C(23)	1.3247(18)	C(38)-C(39)	1.5086(17)
C(23)-C(24)	1.498(2)	C(39)-C(40)	1.5476(16)
C(23)-H(23)	0.9500	C(39)-H(39A)	0.9900
C(24)-H(24A)	0.9800	C(39)-H(39B)	0.9900
C(24)-H(24B)	0.9800	C(40)-C(44)	1.5185(17)
C(24)-H(24C)	0.9800	C(40)-C(42)	1.5290(16)
C(25)-O(7)	1.2022(17)	C(40)-C(41)	1.5507(17)
C(25)-O(8)	1.3261(16)	C(41)-H(41A)	0.9900
C(26)-O(8)	1.4545(17)	C(41)-H(41B)	0.9900
C(26)-H(26A)	0.9800	C(42)-O(13)	1.2012(15)
C(26)-H(26B)	0.9800	C(42)-O(14)	1.3383(15)
C(26)-H(26C)	0.9800	C(43)-O(14)	1.4462(15)
C(27)-O(9)	1.1982(15)	C(43)-H(43A)	0.9800
C(27)-O(10)	1.3432(14)	C(43)-H(43B)	0.9800
C(28)-O(10)	1.4424(16)	C(43)-H(43C)	0.9800
C(28)-H(28A)	0.9800	C(44)-O(15)	1.2005(15)

C(44)-O(16)	1.3469(16)	C(60)-H(60B)	0.9800
C(45)-O(16)	1.4442(16)	C(60)-H(60C)	0.9800
C(45)-H(45A)	0.9800	C(61)-H(61A)	0.9800
C(45)-H(45B)	0.9800	C(61)-H(61B)	0.9800
C(45)-H(45C)	0.9800	C(61)-H(61C)	0.9800
C(46)-C(50)	1.5307(16)	C(62)-H(62A)	0.9800
C(46)-C(47)	1.5489(16)	C(62)-H(62B)	0.9800
C(46)-H(46)	1.0000	C(62)-H(62C)	0.9800
C(47)-C(48)	1.5448(16)	C(63)-C(65)	1.5103(18)
C(47)-H(47A)	0.9900	C(63)-C(64)	1.5413(17)
C(47)-H(47B)	0.9900	C(63)-H(63)	1.0000
C(48)-C(55)	1.5186(16)	C(64)-H(64A)	0.9800
C(48)-C(53)	1.5190(17)	C(64)-H(64B)	0.9800
C(48)-C(49)	1.5393(17)	C(64)-H(64C)	0.9800
C(49)-C(50)	1.5101(16)	C(65)-C(66)	1.3431(16)
C(49)-H(49A)	0.9900	C(65)-C(69)	1.5142(17)
C(49)-H(49B)	0.9900	C(66)-C(74)	1.5037(16)
C(50)-C(51)	1.3250(18)	C(66)-C(67)	1.5092(17)
C(51)-C(52)	1.499(2)	C(67)-C(68)	1.5496(16)
C(51)-H(51)	0.9500	C(67)-H(67A)	0.9900
C(52)-H(52A)	0.9800	C(67)-H(67B)	0.9900
C(52)-H(52B)	0.9800	C(68)-C(72)	1.5196(17)
C(52)-H(52C)	0.9800	C(68)-C(70)	1.5291(17)
C(53)-O(17)	1.1941(15)	C(68)-C(69)	1.5489(18)
C(53)-O(18)	1.3381(14)	C(69)-H(69A)	0.9900
C(54)-O(18)	1.4425(16)	C(69)-H(69B)	0.9900
C(54)-H(54A)	0.9800	C(70)-O(23)	1.2001(15)
C(54)-H(54B)	0.9800	C(70)-O(24)	1.3405(14)
C(54)-H(54C)	0.9800	C(71)-O(24)	1.4460(16)
C(55)-O(19)	1.2003(16)	C(71)-H(71A)	0.9800
C(55)-O(20)	1.3373(15)	C(71)-H(71B)	0.9800
C(56)-O(20)	1.4473(15)	C(71)-H(71C)	0.9800
C(56)-H(56A)	0.9800	C(72)-O(25)	1.1993(15)
C(56)-H(56B)	0.9800	C(72)-O(26)	1.3410(17)
C(56)-H(56C)	0.9800	C(73)-O(26)	1.4454(17)
C(57)-O(21)	1.4668(15)	C(73)-H(73A)	0.9800
C(57)-C(60)	1.5167(17)	C(73)-H(73B)	0.9800
C(57)-C(59)	1.5221(19)	C(73)-H(73C)	0.9800
C(57)-C(58)	1.5556(17)	C(74)-C(78)	1.5323(16)
C(58)-O(22)	1.4668(14)	C(74)-C(75)	1.5452(16)
C(58)-C(62)	1.5131(18)	C(74)-H(74)	1.0000
C(58)-C(61)	1.5239(19)	C(75)-C(76)	1.5419(15)
C(59)-H(59A)	0.9800	C(75)-H(75A)	0.9900
C(59)-H(59B)	0.9800	C(75)-H(75B)	0.9900
C(59)-H(59C)	0.9800	C(76)-C(81)	1.5203(17)
C(60)-H(60A)	0.9800	C(76)-C(83)	1.5263(16)

C(76)-C(77)	1.5358(16)	C(1)-C(3)-H(3C)	109.5
C(77)-C(78)	1.5113(16)	H(3A)-C(3)-H(3C)	109.5
C(77)-H(77A)	0.9900	H(3B)-C(3)-H(3C)	109.5
C(77)-H(77B)	0.9900	C(1)-C(4)-H(4A)	109.5
C(78)-C(79)	1.3261(17)	C(1)-C(4)-H(4B)	109.5
C(79)-C(80)	1.5043(18)	H(4A)-C(4)-H(4B)	109.5
C(79)-H(79)	0.9500	C(1)-C(4)-H(4C)	109.5
C(80)-H(80A)	0.9800	H(4A)-C(4)-H(4C)	109.5
C(80)-H(80B)	0.9800	H(4B)-C(4)-H(4C)	109.5
C(80)-H(80C)	0.9800	C(2)-C(5)-H(5A)	109.5
C(81)-O(27)	1.2024(15)	C(2)-C(5)-H(5B)	109.5
C(81)-O(28)	1.3461(14)	H(5A)-C(5)-H(5B)	109.5
C(82)-O(28)	1.4408(16)	C(2)-C(5)-H(5C)	109.5
C(82)-H(82A)	0.9800	H(5A)-C(5)-H(5C)	109.5
C(82)-H(82B)	0.9800	H(5B)-C(5)-H(5C)	109.5
C(82)-H(82C)	0.9800	C(2)-C(6)-H(6A)	109.5
C(83)-O(29)	1.1964(16)	C(2)-C(6)-H(6B)	109.5
C(83)-O(30)	1.3343(15)	H(6A)-C(6)-H(6B)	109.5
C(84)-O(30)	1.4458(15)	C(2)-C(6)-H(6C)	109.5
C(84)-H(84A)	0.9800	H(6A)-C(6)-H(6C)	109.5
C(84)-H(84B)	0.9800	H(6B)-C(6)-H(6C)	109.5
C(84)-H(84C)	0.9800	C(9)-C(7)-C(8)	112.57(10)
O(2)-B(1)-O(1)	113.59(11)	C(9)-C(7)-B(1)	107.21(9)
O(2)-B(1)-C(7)	122.97(11)	C(8)-C(7)-B(1)	112.13(10)
O(1)-B(1)-C(7)	123.41(11)	C(9)-C(7)-H(7)	108.3
O(11)-B(2)-O(12)	113.47(11)	C(8)-C(7)-H(7)	108.3
O(11)-B(2)-C(35)	123.49(11)	B(1)-C(7)-H(7)	108.3
O(12)-B(2)-C(35)	122.99(12)	C(7)-C(8)-H(8A)	109.5
O(22)-B(3)-O(21)	113.56(11)	C(7)-C(8)-H(8B)	109.5
O(22)-B(3)-C(63)	123.30(11)	H(8A)-C(8)-H(8B)	109.5
O(21)-B(3)-C(63)	123.11(11)	C(7)-C(8)-H(8C)	109.5
O(1)-C(1)-C(4)	109.30(10)	H(8A)-C(8)-H(8C)	109.5
O(1)-C(1)-C(3)	106.53(10)	H(8B)-C(8)-H(8C)	109.5
C(4)-C(1)-C(3)	110.23(11)	C(10)-C(9)-C(7)	127.66(11)
O(1)-C(1)-C(2)	102.06(9)	C(10)-C(9)-C(13)	111.75(10)
C(4)-C(1)-C(2)	114.79(11)	C(7)-C(9)-C(13)	120.55(10)
C(3)-C(1)-C(2)	113.24(11)	C(9)-C(10)-C(18)	128.71(11)
O(2)-C(2)-C(5)	109.32(10)	C(9)-C(10)-C(11)	111.77(10)
O(2)-C(2)-C(6)	106.35(10)	C(18)-C(10)-C(11)	119.52(10)
C(5)-C(2)-C(6)	110.50(12)	C(10)-C(11)-C(12)	103.88(9)
O(2)-C(2)-C(1)	102.16(9)	C(10)-C(11)-H(11A)	111.0
C(5)-C(2)-C(1)	115.18(11)	C(12)-C(11)-H(11A)	111.0
C(6)-C(2)-C(1)	112.60(11)	C(10)-C(11)-H(11B)	111.0
C(1)-C(3)-H(3A)	109.5	C(12)-C(11)-H(11B)	111.0
C(1)-C(3)-H(3B)	109.5	H(11A)-C(11)-H(11B)	109.0
H(3A)-C(3)-H(3B)	109.5	C(16)-C(12)-C(14)	108.33(10)

C(16)-C(12)-C(11)	110.76(10)	C(21)-C(20)-C(19)	103.47(9)
C(14)-C(12)-C(11)	110.39(9)	C(22)-C(21)-C(20)	104.89(9)
C(16)-C(12)-C(13)	113.54(10)	C(22)-C(21)-H(21A)	110.8
C(14)-C(12)-C(13)	108.51(10)	C(20)-C(21)-H(21A)	110.8
C(11)-C(12)-C(13)	105.27(9)	C(22)-C(21)-H(21B)	110.8
C(9)-C(13)-C(12)	103.86(9)	C(20)-C(21)-H(21B)	110.8
C(9)-C(13)-H(13A)	111.0	H(21A)-C(21)-H(21B)	108.8
C(12)-C(13)-H(13A)	111.0	C(23)-C(22)-C(21)	126.11(11)
C(9)-C(13)-H(13B)	111.0	C(23)-C(22)-C(18)	124.44(11)
C(12)-C(13)-H(13B)	111.0	C(21)-C(22)-C(18)	109.45(10)
H(13A)-C(13)-H(13B)	109.0	C(22)-C(23)-C(24)	125.85(13)
O(3)-C(14)-O(4)	123.99(12)	C(22)-C(23)-H(23)	117.1
O(3)-C(14)-C(12)	125.50(11)	C(24)-C(23)-H(23)	117.1
O(4)-C(14)-C(12)	110.46(10)	C(23)-C(24)-H(24A)	109.5
O(4)-C(15)-H(15A)	109.5	C(23)-C(24)-H(24B)	109.5
O(4)-C(15)-H(15B)	109.5	H(24A)-C(24)-H(24B)	109.5
H(15A)-C(15)-H(15B)	109.5	C(23)-C(24)-H(24C)	109.5
O(4)-C(15)-H(15C)	109.5	H(24A)-C(24)-H(24C)	109.5
H(15A)-C(15)-H(15C)	109.5	H(24B)-C(24)-H(24C)	109.5
H(15B)-C(15)-H(15C)	109.5	O(7)-C(25)-O(8)	123.91(12)
O(5)-C(16)-O(6)	124.24(12)	O(7)-C(25)-C(20)	124.19(12)
O(5)-C(16)-C(12)	126.63(12)	O(8)-C(25)-C(20)	111.82(11)
O(6)-C(16)-C(12)	109.10(10)	O(8)-C(26)-H(26A)	109.5
O(6)-C(17)-H(17A)	109.5	O(8)-C(26)-H(26B)	109.5
O(6)-C(17)-H(17B)	109.5	H(26A)-C(26)-H(26B)	109.5
H(17A)-C(17)-H(17B)	109.5	O(8)-C(26)-H(26C)	109.5
O(6)-C(17)-H(17C)	109.5	H(26A)-C(26)-H(26C)	109.5
H(17A)-C(17)-H(17C)	109.5	H(26B)-C(26)-H(26C)	109.5
H(17B)-C(17)-H(17C)	109.5	O(9)-C(27)-O(10)	124.22(12)
C(10)-C(18)-C(22)	113.00(10)	O(9)-C(27)-C(20)	125.39(11)
C(10)-C(18)-C(19)	112.40(9)	O(10)-C(27)-C(20)	110.38(10)
C(22)-C(18)-C(19)	104.28(9)	O(10)-C(28)-H(28A)	109.5
C(10)-C(18)-H(18)	109.0	O(10)-C(28)-H(28B)	109.5
C(22)-C(18)-H(18)	109.0	H(28A)-C(28)-H(28B)	109.5
C(19)-C(18)-H(18)	109.0	O(10)-C(28)-H(28C)	109.5
C(20)-C(19)-C(18)	105.05(9)	H(28A)-C(28)-H(28C)	109.5
C(20)-C(19)-H(19A)	110.7	H(28B)-C(28)-H(28C)	109.5
C(18)-C(19)-H(19A)	110.7	O(11)-C(29)-C(32)	108.89(10)
C(20)-C(19)-H(19B)	110.7	O(11)-C(29)-C(31)	106.58(10)
C(18)-C(19)-H(19B)	110.7	C(32)-C(29)-C(31)	110.52(12)
H(19A)-C(19)-H(19B)	108.8	O(11)-C(29)-C(30)	102.06(10)
C(27)-C(20)-C(25)	109.59(10)	C(32)-C(29)-C(30)	115.14(11)
C(27)-C(20)-C(21)	112.09(10)	C(31)-C(29)-C(30)	112.90(11)
C(25)-C(20)-C(21)	111.75(10)	O(12)-C(30)-C(33)	108.94(11)
C(27)-C(20)-C(19)	110.39(10)	O(12)-C(30)-C(34)	106.56(11)
C(25)-C(20)-C(19)	109.40(10)	C(33)-C(30)-C(34)	110.41(12)

O(12)-C(30)-C(29)	101.97(9)	C(38)-C(39)-H(39A)	110.9
C(33)-C(30)-C(29)	115.17(11)	C(40)-C(39)-H(39A)	110.9
C(34)-C(30)-C(29)	113.04(12)	C(38)-C(39)-H(39B)	110.9
C(29)-C(31)-H(31A)	109.5	C(40)-C(39)-H(39B)	110.9
C(29)-C(31)-H(31B)	109.5	H(39A)-C(39)-H(39B)	108.9
H(31A)-C(31)-H(31B)	109.5	C(44)-C(40)-C(42)	107.95(10)
C(29)-C(31)-H(31C)	109.5	C(44)-C(40)-C(39)	110.80(10)
H(31A)-C(31)-H(31C)	109.5	C(42)-C(40)-C(39)	110.31(9)
H(31B)-C(31)-H(31C)	109.5	C(44)-C(40)-C(41)	113.39(10)
C(29)-C(32)-H(32A)	109.5	C(42)-C(40)-C(41)	109.03(10)
C(29)-C(32)-H(32B)	109.5	C(39)-C(40)-C(41)	105.34(9)
H(32A)-C(32)-H(32B)	109.5	C(37)-C(41)-C(40)	104.04(9)
C(29)-C(32)-H(32C)	109.5	C(37)-C(41)-H(41A)	110.9
H(32A)-C(32)-H(32C)	109.5	C(40)-C(41)-H(41A)	110.9
H(32B)-C(32)-H(32C)	109.5	C(37)-C(41)-H(41B)	110.9
C(30)-C(33)-H(33A)	109.5	C(40)-C(41)-H(41B)	110.9
C(30)-C(33)-H(33B)	109.5	H(41A)-C(41)-H(41B)	109.0
H(33A)-C(33)-H(33B)	109.5	O(13)-C(42)-O(14)	123.82(11)
C(30)-C(33)-H(33C)	109.5	O(13)-C(42)-C(40)	125.59(11)
H(33A)-C(33)-H(33C)	109.5	O(14)-C(42)-C(40)	110.57(10)
H(33B)-C(33)-H(33C)	109.5	O(14)-C(43)-H(43A)	109.5
C(30)-C(34)-H(34A)	109.5	O(14)-C(43)-H(43B)	109.5
C(30)-C(34)-H(34B)	109.5	H(43A)-C(43)-H(43B)	109.5
H(34A)-C(34)-H(34B)	109.5	O(14)-C(43)-H(43C)	109.5
C(30)-C(34)-H(34C)	109.5	H(43A)-C(43)-H(43C)	109.5
H(34A)-C(34)-H(34C)	109.5	H(43B)-C(43)-H(43C)	109.5
H(34B)-C(34)-H(34C)	109.5	O(15)-C(44)-O(16)	124.18(12)
C(37)-C(35)-C(36)	111.92(11)	O(15)-C(44)-C(40)	126.82(12)
C(37)-C(35)-B(2)	106.84(9)	O(16)-C(44)-C(40)	108.96(10)
C(36)-C(35)-B(2)	112.69(10)	O(16)-C(45)-H(45A)	109.5
C(37)-C(35)-H(35)	108.4	O(16)-C(45)-H(45B)	109.5
C(36)-C(35)-H(35)	108.4	H(45A)-C(45)-H(45B)	109.5
B(2)-C(35)-H(35)	108.4	O(16)-C(45)-H(45C)	109.5
C(35)-C(36)-H(36A)	109.5	H(45A)-C(45)-H(45C)	109.5
C(35)-C(36)-H(36B)	109.5	H(45B)-C(45)-H(45C)	109.5
H(36A)-C(36)-H(36B)	109.5	C(38)-C(46)-C(50)	113.41(10)
C(35)-C(36)-H(36C)	109.5	C(38)-C(46)-C(47)	112.28(9)
H(36A)-C(36)-H(36C)	109.5	C(50)-C(46)-C(47)	104.08(9)
H(36B)-C(36)-H(36C)	109.5	C(38)-C(46)-H(46)	109.0
C(38)-C(37)-C(35)	127.46(11)	C(50)-C(46)-H(46)	109.0
C(38)-C(37)-C(41)	111.59(11)	C(47)-C(46)-H(46)	109.0
C(35)-C(37)-C(41)	120.90(10)	C(48)-C(47)-C(46)	105.05(9)
C(37)-C(38)-C(46)	128.34(11)	C(48)-C(47)-H(47A)	110.7
C(37)-C(38)-C(39)	111.98(10)	C(46)-C(47)-H(47A)	110.7
C(46)-C(38)-C(39)	119.68(10)	C(48)-C(47)-H(47B)	110.7
C(38)-C(39)-C(40)	104.13(9)	C(46)-C(47)-H(47B)	110.7

H(47A)-C(47)-H(47B)	108.8	O(21)-C(57)-C(58)	102.08(9)
C(55)-C(48)-C(53)	111.21(10)	C(60)-C(57)-C(58)	114.94(11)
C(55)-C(48)-C(49)	112.97(10)	C(59)-C(57)-C(58)	113.20(11)
C(53)-C(48)-C(49)	108.18(10)	O(22)-C(58)-C(62)	108.98(10)
C(55)-C(48)-C(47)	110.90(9)	O(22)-C(58)-C(61)	106.43(10)
C(53)-C(48)-C(47)	110.44(10)	C(62)-C(58)-C(61)	110.59(11)
C(49)-C(48)-C(47)	102.82(9)	O(22)-C(58)-C(57)	102.07(9)
C(50)-C(49)-C(48)	103.79(9)	C(62)-C(58)-C(57)	115.42(11)
C(50)-C(49)-H(49A)	111.0	C(61)-C(58)-C(57)	112.57(10)
C(48)-C(49)-H(49A)	111.0	C(57)-C(59)-H(59A)	109.5
C(50)-C(49)-H(49B)	111.0	C(57)-C(59)-H(59B)	109.5
C(48)-C(49)-H(49B)	111.0	H(59A)-C(59)-H(59B)	109.5
H(49A)-C(49)-H(49B)	109.0	C(57)-C(59)-H(59C)	109.5
C(51)-C(50)-C(49)	126.11(11)	H(59A)-C(59)-H(59C)	109.5
C(51)-C(50)-C(46)	124.44(11)	H(59B)-C(59)-H(59C)	109.5
C(49)-C(50)-C(46)	109.41(10)	C(57)-C(60)-H(60A)	109.5
C(50)-C(51)-C(52)	126.05(13)	C(57)-C(60)-H(60B)	109.5
C(50)-C(51)-H(51)	117.0	H(60A)-C(60)-H(60B)	109.5
C(52)-C(51)-H(51)	117.0	C(57)-C(60)-H(60C)	109.5
C(51)-C(52)-H(52A)	109.5	H(60A)-C(60)-H(60C)	109.5
C(51)-C(52)-H(52B)	109.5	H(60B)-C(60)-H(60C)	109.5
H(52A)-C(52)-H(52B)	109.5	C(58)-C(61)-H(61A)	109.5
C(51)-C(52)-H(52C)	109.5	C(58)-C(61)-H(61B)	109.5
H(52A)-C(52)-H(52C)	109.5	H(61A)-C(61)-H(61B)	109.5
H(52B)-C(52)-H(52C)	109.5	C(58)-C(61)-H(61C)	109.5
O(17)-C(53)-O(18)	124.02(12)	H(61A)-C(61)-H(61C)	109.5
O(17)-C(53)-C(48)	124.81(11)	H(61B)-C(61)-H(61C)	109.5
O(18)-C(53)-C(48)	111.02(10)	C(58)-C(62)-H(62A)	109.5
O(18)-C(54)-H(54A)	109.5	C(58)-C(62)-H(62B)	109.5
O(18)-C(54)-H(54B)	109.5	H(62A)-C(62)-H(62B)	109.5
H(54A)-C(54)-H(54B)	109.5	C(58)-C(62)-H(62C)	109.5
O(18)-C(54)-H(54C)	109.5	H(62A)-C(62)-H(62C)	109.5
H(54A)-C(54)-H(54C)	109.5	H(62B)-C(62)-H(62C)	109.5
H(54B)-C(54)-H(54C)	109.5	C(65)-C(63)-C(64)	112.15(11)
O(19)-C(55)-O(20)	124.64(12)	C(65)-C(63)-B(3)	107.18(10)
O(19)-C(55)-C(48)	125.39(12)	C(64)-C(63)-B(3)	112.02(10)
O(20)-C(55)-C(48)	109.90(10)	C(65)-C(63)-H(63)	108.5
O(20)-C(56)-H(56A)	109.5	C(64)-C(63)-H(63)	108.5
O(20)-C(56)-H(56B)	109.5	B(3)-C(63)-H(63)	108.5
H(56A)-C(56)-H(56B)	109.5	C(63)-C(64)-H(64A)	109.5
O(20)-C(56)-H(56C)	109.5	C(63)-C(64)-H(64B)	109.5
H(56A)-C(56)-H(56C)	109.5	H(64A)-C(64)-H(64B)	109.5
H(56B)-C(56)-H(56C)	109.5	C(63)-C(64)-H(64C)	109.5
O(21)-C(57)-C(60)	108.77(10)	H(64A)-C(64)-H(64C)	109.5
O(21)-C(57)-C(59)	106.80(10)	H(64B)-C(64)-H(64C)	109.5
C(60)-C(57)-C(59)	110.34(11)	C(66)-C(65)-C(63)	127.81(11)

C(66)-C(65)-C(69)	111.33(11)	C(75)-C(74)-H(74)	109.1
C(63)-C(65)-C(69)	120.82(10)	C(76)-C(75)-C(74)	104.81(9)
C(65)-C(66)-C(74)	128.30(11)	C(76)-C(75)-H(75A)	110.8
C(65)-C(66)-C(67)	112.10(10)	C(74)-C(75)-H(75A)	110.8
C(74)-C(66)-C(67)	119.60(10)	C(76)-C(75)-H(75B)	110.8
C(66)-C(67)-C(68)	103.86(9)	C(74)-C(75)-H(75B)	110.8
C(66)-C(67)-H(67A)	111.0	H(75A)-C(75)-H(75B)	108.9
C(68)-C(67)-H(67A)	111.0	C(81)-C(76)-C(83)	108.79(9)
C(66)-C(67)-H(67B)	111.0	C(81)-C(76)-C(77)	111.78(9)
C(68)-C(67)-H(67B)	111.0	C(83)-C(76)-C(77)	112.55(10)
H(67A)-C(67)-H(67B)	109.0	C(81)-C(76)-C(75)	110.46(10)
C(72)-C(68)-C(70)	107.65(10)	C(83)-C(76)-C(75)	110.02(9)
C(72)-C(68)-C(69)	113.78(10)	C(77)-C(76)-C(75)	103.14(9)
C(70)-C(68)-C(69)	108.88(10)	C(78)-C(77)-C(76)	104.02(9)
C(72)-C(68)-C(67)	110.66(10)	C(78)-C(77)-H(77A)	111.0
C(70)-C(68)-C(67)	110.66(9)	C(76)-C(77)-H(77A)	111.0
C(69)-C(68)-C(67)	105.21(10)	C(78)-C(77)-H(77B)	111.0
C(65)-C(69)-C(68)	104.01(9)	C(76)-C(77)-H(77B)	111.0
C(65)-C(69)-H(69A)	111.0	H(77A)-C(77)-H(77B)	109.0
C(68)-C(69)-H(69A)	111.0	C(79)-C(78)-C(77)	125.77(11)
C(65)-C(69)-H(69B)	111.0	C(79)-C(78)-C(74)	124.93(11)
C(68)-C(69)-H(69B)	111.0	C(77)-C(78)-C(74)	109.30(9)
H(69A)-C(69)-H(69B)	109.0	C(78)-C(79)-C(80)	125.37(12)
O(23)-C(70)-O(24)	124.05(12)	C(78)-C(79)-H(79)	117.3
O(23)-C(70)-C(68)	125.73(11)	C(80)-C(79)-H(79)	117.3
O(24)-C(70)-C(68)	110.21(10)	C(79)-C(80)-H(80A)	109.5
O(24)-C(71)-H(71A)	109.5	C(79)-C(80)-H(80B)	109.5
O(24)-C(71)-H(71B)	109.5	H(80A)-C(80)-H(80B)	109.5
H(71A)-C(71)-H(71B)	109.5	C(79)-C(80)-H(80C)	109.5
O(24)-C(71)-H(71C)	109.5	H(80A)-C(80)-H(80C)	109.5
H(71A)-C(71)-H(71C)	109.5	H(80B)-C(80)-H(80C)	109.5
H(71B)-C(71)-H(71C)	109.5	O(27)-C(81)-O(28)	124.26(12)
O(25)-C(72)-O(26)	124.20(12)	O(27)-C(81)-C(76)	125.97(11)
O(25)-C(72)-C(68)	126.64(13)	O(28)-C(81)-C(76)	109.77(10)
O(26)-C(72)-C(68)	109.14(10)	O(28)-C(82)-H(82A)	109.5
O(26)-C(73)-H(73A)	109.5	O(28)-C(82)-H(82B)	109.5
O(26)-C(73)-H(73B)	109.5	H(82A)-C(82)-H(82B)	109.5
H(73A)-C(73)-H(73B)	109.5	O(28)-C(82)-H(82C)	109.5
O(26)-C(73)-H(73C)	109.5	H(82A)-C(82)-H(82C)	109.5
H(73A)-C(73)-H(73C)	109.5	H(82B)-C(82)-H(82C)	109.5
H(73B)-C(73)-H(73C)	109.5	O(29)-C(83)-O(30)	125.27(12)
C(66)-C(74)-C(78)	113.32(10)	O(29)-C(83)-C(76)	125.11(12)
C(66)-C(74)-C(75)	111.97(9)	O(30)-C(83)-C(76)	109.55(10)
C(78)-C(74)-C(75)	104.12(9)	O(30)-C(84)-H(84A)	109.5
C(66)-C(74)-H(74)	109.1	O(30)-C(84)-H(84B)	109.5
C(78)-C(74)-H(74)	109.1	H(84A)-C(84)-H(84B)	109.5

O(30)-C(84)-H(84C)	109.5	C(42)-O(14)-C(43)	115.62(10)
H(84A)-C(84)-H(84C)	109.5	C(44)-O(16)-C(45)	116.90(11)
H(84B)-C(84)-H(84C)	109.5	C(53)-O(18)-C(54)	116.36(10)
B(1)-O(1)-C(1)	106.22(9)	C(55)-O(20)-C(56)	116.54(11)
B(1)-O(2)-C(2)	106.56(9)	B(3)-O(21)-C(57)	106.27(9)
C(14)-O(4)-C(15)	115.98(11)	B(3)-O(22)-C(58)	106.77(9)
C(16)-O(6)-C(17)	116.71(11)	C(70)-O(24)-C(71)	116.01(10)
C(25)-O(8)-C(26)	115.96(12)	C(72)-O(26)-C(73)	116.95(11)
C(27)-O(10)-C(28)	116.02(10)	C(81)-O(28)-C(82)	116.17(11)
B(2)-O(11)-C(29)	106.72(9)	C(83)-O(30)-C(84)	117.09(11)
B(2)-O(12)-C(30)	106.28(10)		

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for **26b**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
B(1)	14(1)	23(1)	14(1)	2(1)	3(1)	2(1)
B(2)	17(1)	22(1)	14(1)	1(1)	4(1)	3(1)
B(3)	17(1)	21(1)	14(1)	-2(1)	4(1)	-3(1)
C(1)	15(1)	23(1)	18(1)	-2(1)	6(1)	1(1)
C(2)	17(1)	20(1)	25(1)	-2(1)	10(1)	0(1)
C(3)	22(1)	35(1)	32(1)	-5(1)	0(1)	10(1)
C(4)	34(1)	35(1)	22(1)	-7(1)	14(1)	-3(1)
C(5)	45(1)	22(1)	50(1)	-1(1)	32(1)	-3(1)
C(6)	18(1)	36(1)	37(1)	-11(1)	-2(1)	2(1)
C(7)	16(1)	21(1)	16(1)	0(1)	5(1)	3(1)
C(8)	29(1)	22(1)	24(1)	6(1)	5(1)	7(1)
C(9)	15(1)	17(1)	15(1)	1(1)	5(1)	1(1)
C(10)	16(1)	18(1)	16(1)	0(1)	7(1)	-1(1)
C(11)	15(1)	25(1)	14(1)	0(1)	5(1)	-2(1)
C(12)	14(1)	20(1)	16(1)	1(1)	5(1)	-2(1)
C(13)	17(1)	24(1)	16(1)	3(1)	6(1)	0(1)
C(14)	16(1)	24(1)	16(1)	0(1)	4(1)	0(1)
C(15)	24(1)	36(1)	32(1)	-11(1)	9(1)	4(1)
C(16)	16(1)	23(1)	19(1)	-2(1)	8(1)	-2(1)
C(17)	20(1)	47(1)	27(1)	-3(1)	3(1)	-13(1)
C(18)	17(1)	19(1)	16(1)	1(1)	7(1)	0(1)
C(19)	20(1)	18(1)	18(1)	-1(1)	9(1)	-1(1)
C(20)	15(1)	17(1)	15(1)	1(1)	5(1)	-1(1)
C(21)	23(1)	21(1)	15(1)	-2(1)	6(1)	-7(1)
C(22)	21(1)	20(1)	17(1)	-1(1)	10(1)	-1(1)
C(23)	45(1)	20(1)	28(1)	0(1)	21(1)	0(1)
C(24)	78(1)	23(1)	41(1)	-12(1)	34(1)	-11(1)
C(25)	24(1)	23(1)	23(1)	5(1)	12(1)	1(1)

C(26)	52(1)	19(1)	41(1)	7(1)	22(1)	7(1)
C(27)	18(1)	19(1)	18(1)	0(1)	6(1)	-1(1)
C(28)	20(1)	39(1)	32(1)	0(1)	15(1)	1(1)
C(29)	21(1)	23(1)	19(1)	-5(1)	7(1)	-1(1)
C(30)	18(1)	25(1)	21(1)	-7(1)	6(1)	0(1)
C(31)	18(1)	37(1)	27(1)	-5(1)	2(1)	1(1)
C(32)	44(1)	26(1)	35(1)	-3(1)	21(1)	-6(1)
C(33)	30(1)	43(1)	24(1)	-14(1)	14(1)	-6(1)
C(34)	27(1)	33(1)	37(1)	-9(1)	-2(1)	10(1)
C(35)	19(1)	19(1)	16(1)	1(1)	6(1)	5(1)
C(36)	34(1)	22(1)	25(1)	6(1)	6(1)	8(1)
C(37)	19(1)	14(1)	16(1)	-1(1)	7(1)	2(1)
C(38)	17(1)	14(1)	15(1)	-1(1)	6(1)	0(1)
C(39)	18(1)	21(1)	14(1)	1(1)	6(1)	-1(1)
C(40)	16(1)	18(1)	17(1)	0(1)	7(1)	0(1)
C(41)	20(1)	22(1)	16(1)	4(1)	8(1)	3(1)
C(42)	15(1)	21(1)	17(1)	-1(1)	5(1)	0(1)
C(43)	25(1)	30(1)	31(1)	-10(1)	11(1)	4(1)
C(44)	18(1)	21(1)	22(1)	-3(1)	10(1)	-1(1)
C(45)	20(1)	41(1)	26(1)	-5(1)	5(1)	-11(1)
C(46)	18(1)	17(1)	15(1)	-1(1)	8(1)	1(1)
C(47)	20(1)	17(1)	16(1)	-1(1)	8(1)	0(1)
C(48)	14(1)	17(1)	15(1)	1(1)	5(1)	0(1)
C(49)	18(1)	20(1)	16(1)	-1(1)	4(1)	-2(1)
C(50)	21(1)	19(1)	16(1)	-2(1)	10(1)	0(1)
C(51)	58(1)	20(1)	22(1)	-3(1)	18(1)	-3(1)
C(52)	97(2)	24(1)	26(1)	-8(1)	21(1)	-9(1)
C(53)	17(1)	22(1)	17(1)	0(1)	6(1)	0(1)
C(54)	24(1)	36(1)	36(1)	2(1)	20(1)	5(1)
C(55)	19(1)	19(1)	19(1)	2(1)	7(1)	0(1)
C(56)	41(1)	16(1)	30(1)	2(1)	12(1)	1(1)
C(57)	17(1)	20(1)	19(1)	3(1)	7(1)	0(1)
C(58)	17(1)	20(1)	20(1)	1(1)	7(1)	0(1)
C(59)	21(1)	29(1)	33(1)	4(1)	3(1)	-6(1)
C(60)	28(1)	33(1)	23(1)	8(1)	13(1)	3(1)
C(61)	17(1)	32(1)	29(1)	1(1)	1(1)	-1(1)
C(62)	32(1)	23(1)	36(1)	-1(1)	17(1)	3(1)
C(63)	22(1)	19(1)	16(1)	-2(1)	7(1)	-4(1)
C(64)	41(1)	21(1)	24(1)	-6(1)	10(1)	-8(1)
C(65)	21(1)	15(1)	17(1)	0(1)	9(1)	1(1)
C(66)	19(1)	16(1)	15(1)	1(1)	8(1)	3(1)
C(67)	18(1)	24(1)	15(1)	0(1)	7(1)	4(1)
C(68)	18(1)	21(1)	17(1)	1(1)	8(1)	5(1)
C(69)	22(1)	24(1)	17(1)	-4(1)	9(1)	2(1)
C(70)	16(1)	23(1)	16(1)	2(1)	5(1)	4(1)
C(71)	22(1)	33(1)	30(1)	10(1)	12(1)	2(1)

C(72)	21(1)	24(1)	21(1)	5(1)	11(1)	6(1)
C(73)	26(1)	50(1)	28(1)	8(1)	5(1)	20(1)
C(74)	19(1)	16(1)	13(1)	1(1)	7(1)	1(1)
C(75)	23(1)	16(1)	18(1)	1(1)	11(1)	2(1)
C(76)	17(1)	15(1)	16(1)	-1(1)	7(1)	1(1)
C(77)	20(1)	19(1)	14(1)	0(1)	5(1)	5(1)
C(78)	18(1)	17(1)	15(1)	0(1)	8(1)	1(1)
C(79)	35(1)	18(1)	20(1)	1(1)	13(1)	1(1)
C(80)	47(1)	19(1)	25(1)	6(1)	14(1)	4(1)
C(81)	19(1)	14(1)	19(1)	0(1)	8(1)	1(1)
C(82)	23(1)	27(1)	48(1)	3(1)	23(1)	0(1)
C(83)	20(1)	18(1)	22(1)	-3(1)	9(1)	0(1)
C(84)	40(1)	16(1)	35(1)	-5(1)	14(1)	0(1)
O(1)	20(1)	23(1)	21(1)	-4(1)	11(1)	-4(1)
O(2)	21(1)	21(1)	23(1)	-1(1)	13(1)	0(1)
O(3)	32(1)	21(1)	34(1)	2(1)	14(1)	-1(1)
O(4)	26(1)	28(1)	26(1)	-2(1)	15(1)	1(1)
O(5)	24(1)	25(1)	30(1)	4(1)	10(1)	-6(1)
O(6)	17(1)	34(1)	24(1)	4(1)	0(1)	-8(1)
O(7)	25(1)	42(1)	49(1)	22(1)	-1(1)	2(1)
O(8)	32(1)	17(1)	35(1)	3(1)	12(1)	-1(1)
O(9)	20(1)	43(1)	22(1)	-4(1)	4(1)	-3(1)
O(10)	18(1)	32(1)	18(1)	-2(1)	9(1)	-1(1)
O(11)	23(1)	23(1)	19(1)	-3(1)	10(1)	0(1)
O(12)	21(1)	26(1)	21(1)	-7(1)	10(1)	-3(1)
O(13)	32(1)	20(1)	34(1)	1(1)	16(1)	-1(1)
O(14)	27(1)	24(1)	25(1)	-3(1)	15(1)	3(1)
O(15)	26(1)	24(1)	37(1)	3(1)	16(1)	-4(1)
O(16)	19(1)	30(1)	25(1)	1(1)	2(1)	-7(1)
O(17)	21(1)	62(1)	26(1)	13(1)	6(1)	12(1)
O(18)	21(1)	29(1)	21(1)	3(1)	12(1)	4(1)
O(19)	28(1)	29(1)	37(1)	11(1)	-5(1)	0(1)
O(20)	26(1)	16(1)	25(1)	1(1)	4(1)	-1(1)
O(21)	20(1)	21(1)	21(1)	4(1)	11(1)	3(1)
O(22)	20(1)	21(1)	21(1)	1(1)	11(1)	-1(1)
O(23)	30(1)	21(1)	33(1)	0(1)	16(1)	4(1)
O(24)	26(1)	27(1)	26(1)	4(1)	16(1)	5(1)
O(25)	31(1)	24(1)	38(1)	1(1)	17(1)	9(1)
O(26)	22(1)	36(1)	25(1)	1(1)	3(1)	14(1)
O(27)	20(1)	38(1)	24(1)	-1(1)	3(1)	-1(1)
O(28)	20(1)	28(1)	24(1)	4(1)	13(1)	2(1)
O(29)	26(1)	29(1)	43(1)	-12(1)	-2(1)	0(1)
O(30)	27(1)	14(1)	29(1)	-2(1)	7(1)	2(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for **26b**.

	x	y	z	U(eq)
H(3A)	5716	8353	1732	46
H(3B)	5273	7501	1701	46
H(3C)	5321	8272	2128	46
H(4A)	4528	8907	630	43
H(4B)	4703	7862	774	43
H(4C)	5220	8610	820	43
H(5A)	4383	7532	2055	53
H(5B)	4154	7164	1479	53
H(5C)	3686	7604	1747	53
H(6A)	3312	8865	1180	48
H(6B)	3635	8402	793	48
H(6C)	3758	9454	949	48
H(7)	4444	10870	2374	21
H(8A)	4786	12216	2049	38
H(8B)	4298	11696	1602	38
H(8C)	4998	11615	1639	38
H(11A)	6272	9929	3525	21
H(11B)	6275	11030	3555	21
H(13A)	5987	11553	2348	22
H(13B)	5924	10546	2097	22
H(15A)	7311	8382	2550	46
H(15B)	7463	8893	2081	46
H(15C)	6803	8492	2017	46
H(17A)	8190	11311	3403	48
H(17B)	8154	11105	3972	48
H(17C)	7827	11989	3671	48
H(18)	4633	10408	3156	20
H(19A)	4810	8887	3291	21
H(19B)	5511	9033	3587	21
H(21A)	4997	10414	4545	24
H(21B)	5648	10088	4507	24
H(23)	5188	12053	3589	35
H(24A)	5361	11878	4672	65
H(24B)	5003	12717	4348	65
H(24C)	5713	12624	4434	65
H(26A)	5358	6589	4356	53
H(26B)	4783	6482	4570	53
H(26C)	5363	7028	4896	53
H(28A)	3266	9706	4071	43
H(28B)	3432	9722	4683	43
H(28C)	3363	8766	4385	43

H(31A)	-10	9196	7863	42
H(31B)	299	8731	7468	42
H(31C)	455	9767	7646	42
H(32A)	1023	7754	8709	50
H(32B)	758	7434	8126	50
H(32C)	325	7902	8421	50
H(33A)	1219	9192	7318	46
H(33B)	1356	8129	7437	46
H(33C)	1900	8838	7505	46
H(34A)	2376	8492	8412	52
H(34B)	1902	7677	8361	52
H(34C)	1975	8425	8804	52
H(35)	1214	11063	9116	22
H(36A)	1636	12389	8838	41
H(36B)	1118	11964	8375	41
H(36C)	1811	11795	8406	41
H(39A)	2974	9807	10215	21
H(39B)	3055	10896	10300	21
H(41A)	2795	11566	9107	22
H(41B)	2671	10589	8822	22
H(43A)	3985	8288	9212	42
H(43B)	4114	8794	8731	42
H(43C)	3455	8413	8693	42
H(45A)	4964	11024	10118	44
H(45B)	4953	10680	10674	44
H(45C)	4662	11646	10463	44
H(46)	1387	10605	9893	19
H(47A)	1393	9055	9926	20
H(47B)	2106	9001	10198	20
H(49A)	1850	10280	11304	22
H(49B)	2426	9848	11165	22
H(51)	2009	12068	10426	38
H(52A)	1861	12502	11260	72
H(52B)	2555	12528	11269	72
H(52C)	2294	11664	11498	72
H(54A)	254	10275	11253	45
H(54B)	101	9250	11381	45
H(54C)	-55	9587	10799	45
H(56A)	1857	6604	10902	42
H(56B)	1150	6403	10699	42
H(56C)	1435	6765	11271	42
H(59A)	5919	3607	9941	43
H(59B)	6377	2772	9981	43
H(59C)	6319	3535	9548	43
H(60A)	7088	4233	11042	41
H(60B)	6924	3181	10911	41

H(60C)	6398	3920	10850	41
H(61A)	8317	4206	10508	40
H(61B)	8000	3716	10891	40
H(61C)	7857	4766	10737	40
H(62A)	7270	2827	9632	43
H(62B)	7501	2468	10210	43
H(62C)	7965	2921	9942	43
H(63)	7179	6168	9297	22
H(64A)	6778	7492	9597	42
H(64B)	7263	7005	10060	42
H(64C)	6560	6876	9998	42
H(67A)	5413	5045	8130	22
H(67B)	5369	6141	8060	22
H(69A)	5597	6784	9244	24
H(69B)	5679	5807	9530	24
H(71A)	4346	3552	9102	41
H(71B)	4168	4087	9553	41
H(71C)	4834	3693	9644	41
H(73A)	3432	6315	8198	53
H(73B)	3446	5968	7644	53
H(73C)	3744	6929	7857	53
H(74)	7027	5708	8513	19
H(75A)	6950	4160	8462	21
H(75B)	6246	4184	8155	21
H(77A)	6653	5453	7112	21
H(77B)	6037	5063	7198	21
H(79)	6429	7233	7975	28
H(80A)	6634	7654	7153	45
H(80B)	5935	7718	7124	45
H(80C)	6188	6837	6903	45
H(82A)	8452	4987	7649	45
H(82B)	8281	4995	7037	45
H(82C)	8406	4045	7341	45
H(84A)	6507	1770	7466	45
H(84B)	7211	1541	7627	45
H(84C)	6888	1909	7062	45

Tetramethyl 1,3,6,8-tetrahydro-*as*-indacene-2,2,7,7-tetracarboxylate (28a)

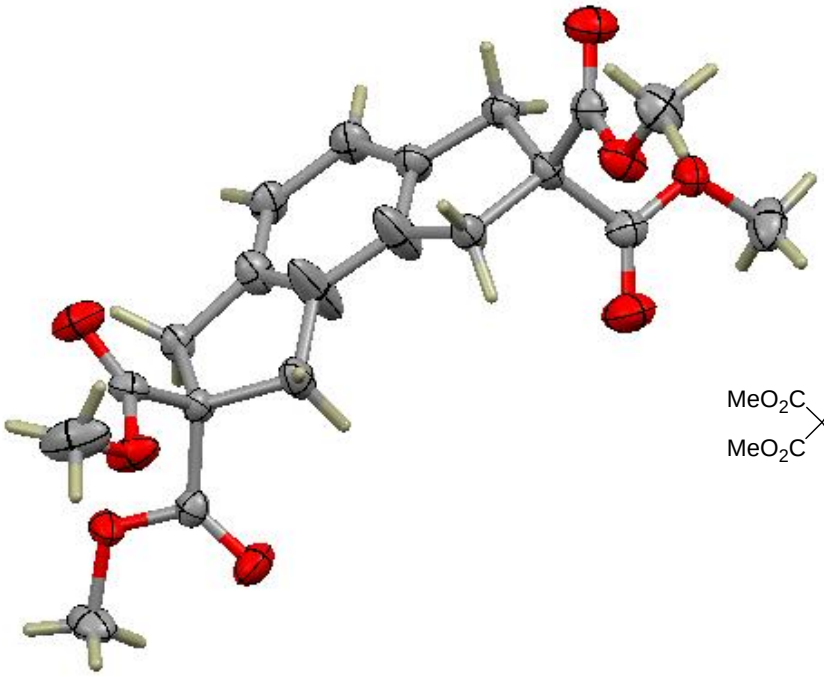


Table 1. Crystal data and structure refinement for **28a**.

Empirical formula	C20 H22 O8	
Formula weight	390.38	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)/c	
Unit cell dimensions	a = 7.8517(7) Å	α= 90°.
	b = 24.562(2) Å	β= 101.179(5)°.
	c = 10.2541(9) Å	γ = 90°.
Volume	1940.0(3) $Å^3$	
Z	4	
Density (calculated)	1.337 Mg/m^3	
Absorption coefficient	0.104 mm^{-1}	
F(000)	824	
Crystal size	0.35 x 0.25 x 0.10 mm^3	
Theta range for data collection	1.66 to 26.02°.	
Index ranges	-9<=h<=7, -30<=k<=30, -11<=l<=12	
Reflections collected	12357	
Independent reflections	3656 [R(int) = 0.0327]	

Completeness to theta = 26.02°	95.6 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9897 and 0.9646
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3656 / 0 / 257
Goodness-of-fit on F^2	1.093
Final R indices [I>2sigma(I)]	R1 = 0.0722, wR2 = 0.2078
R indices (all data)	R1 = 0.0862, wR2 = 0.2326
Largest diff. peak and hole	0.945 and -0.552 e.$Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **28a**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	8178(4)	6421(1)	4289(3)	26(1)
C(2)	8680(4)	6089(1)	5598(3)	27(1)
C(3)	8028(4)	5526(1)	5209(3)	31(1)
C(4)	7529(6)	5481(2)	3843(4)	55(1)
C(5)	7854(4)	5990(1)	3163(3)	32(1)
C(6)	8011(4)	5082(1)	6086(3)	32(1)
C(7)	7312(4)	4567(1)	5492(3)	31(1)
C(8)	6800(4)	4530(1)	4124(3)	31(1)
C(9)	6925(8)	4969(2)	3256(4)	73(2)
C(10)	5932(4)	4867(1)	1933(3)	33(1)
C(11)	5630(3)	4239(1)	1878(3)	24(1)
C(12)	6000(4)	4046(1)	3352(3)	26(1)
C(13)	9651(4)	6809(1)	4112(3)	29(1)
C(14)	10598(5)	7422(2)	2640(4)	44(1)
C(15)	6550(4)	6762(1)	4307(3)	30(1)
C(16)	5295(5)	7431(1)	5482(4)	47(1)
C(17)	6882(3)	3976(1)	1109(3)	25(1)
C(18)	7511(5)	3851(2)	-1021(4)	57(1)
C(19)	3796(4)	4096(1)	1190(3)	25(1)
C(20)	1875(4)	3361(2)	577(4)	39(1)
O(1)	10970(3)	6881(1)	4897(2)	43(1)
O(2)	9254(3)	7062(1)	2942(2)	39(1)
O(3)	5214(3)	6716(1)	3518(3)	53(1)
O(4)	6790(3)	7103(1)	5326(2)	37(1)
O(5)	8210(3)	3750(1)	1592(2)	41(1)
O(6)	6349(3)	4046(1)	-194(2)	38(1)
O(7)	2664(3)	4404(1)	728(2)	39(1)
O(8)	3582(2)	3555(1)	1193(2)	31(1)

Table 3. Bond lengths [Å] and angles [°] for **28a**.

C(1)-C(15)	1.530(4)	C(18)-H(18B)	0.9800
C(1)-C(13)	1.535(4)	C(18)-H(18C)	0.9800
C(1)-C(5)	1.552(4)	C(19)-O(7)	1.194(3)
C(1)-C(2)	1.555(4)	C(19)-O(8)	1.337(3)
C(2)-C(3)	1.500(4)	C(20)-O(8)	1.448(3)
C(2)-H(2A)	0.9900	C(20)-H(20A)	0.9800
C(2)-H(2B)	0.9900	C(20)-H(20B)	0.9800
C(3)-C(4)	1.384(5)	C(20)-H(20C)	0.9800
C(3)-C(6)	1.414(4)	C(15)-C(1)-C(13)	108.2(2)
C(4)-C(9)	1.434(5)	C(15)-C(1)-C(5)	111.4(2)
C(4)-C(5)	1.477(5)	C(13)-C(1)-C(5)	110.7(2)
C(5)-H(5A)	0.9900	C(15)-C(1)-C(2)	110.5(2)
C(5)-H(5B)	0.9900	C(13)-C(1)-C(2)	110.9(2)
C(6)-C(7)	1.464(4)	C(5)-C(1)-C(2)	105.1(2)
C(6)-H(6)	0.9500	C(3)-C(2)-C(1)	103.8(2)
C(7)-C(8)	1.385(4)	C(3)-C(2)-H(2A)	111.0
C(7)-H(7)	0.9500	C(1)-C(2)-H(2A)	111.0
C(8)-C(9)	1.412(5)	C(3)-C(2)-H(2B)	111.0
C(8)-C(12)	1.498(4)	C(1)-C(2)-H(2B)	111.0
C(9)-C(10)	1.450(5)	H(2A)-C(2)-H(2B)	109.0
C(10)-C(11)	1.560(4)	C(4)-C(3)-C(6)	123.1(3)
C(10)-H(10A)	0.9900	C(4)-C(3)-C(2)	111.0(3)
C(10)-H(10B)	0.9900	C(6)-C(3)-C(2)	125.9(3)
C(11)-C(19)	1.517(4)	C(3)-C(4)-C(9)	120.0(3)
C(11)-C(17)	1.519(4)	C(3)-C(4)-C(5)	111.6(3)
C(11)-C(12)	1.557(4)	C(9)-C(4)-C(5)	128.1(3)
C(12)-H(12A)	0.9900	C(4)-C(5)-C(1)	104.2(3)
C(12)-H(12B)	0.9900	C(4)-C(5)-H(5A)	110.9
C(13)-O(1)	1.196(4)	C(1)-C(5)-H(5A)	110.9
C(13)-O(2)	1.334(4)	C(4)-C(5)-H(5B)	110.9
C(14)-O(2)	1.456(4)	C(1)-C(5)-H(5B)	110.9
C(14)-H(14A)	0.9800	H(5A)-C(5)-H(5B)	108.9
C(14)-H(14B)	0.9800	C(3)-C(6)-C(7)	116.8(3)
C(14)-H(14C)	0.9800	C(3)-C(6)-H(6)	121.6
C(15)-O(3)	1.199(4)	C(7)-C(6)-H(6)	121.6
C(15)-O(4)	1.325(4)	C(8)-C(7)-C(6)	119.3(3)
C(16)-O(4)	1.457(4)	C(8)-C(7)-H(7)	120.3
C(16)-H(16A)	0.9800	C(6)-C(7)-H(7)	120.3
C(16)-H(16B)	0.9800	C(7)-C(8)-C(9)	123.1(3)
C(16)-H(16C)	0.9800	C(7)-C(8)-C(12)	126.6(3)
C(17)-O(5)	1.200(3)	C(9)-C(8)-C(12)	110.3(3)
C(17)-O(6)	1.332(3)	C(8)-C(9)-C(4)	117.5(3)
C(18)-O(6)	1.443(4)	C(8)-C(9)-C(10)	111.5(3)
C(18)-H(18A)	0.9800	C(4)-C(9)-C(10)	128.2(3)

C(9)-C(10)-C(11)	104.8(3)	O(4)-C(15)-C(1)	111.3(2)
C(9)-C(10)-H(10A)	110.8	O(4)-C(16)-H(16A)	109.5
C(11)-C(10)-H(10A)	110.8	O(4)-C(16)-H(16B)	109.5
C(9)-C(10)-H(10B)	110.8	H(16A)-C(16)-H(16B)	109.5
C(11)-C(10)-H(10B)	110.8	O(4)-C(16)-H(16C)	109.5
H(10A)-C(10)-H(10B)	108.9	H(16A)-C(16)-H(16C)	109.5
C(19)-C(11)-C(17)	108.1(2)	H(16B)-C(16)-H(16C)	109.5
C(19)-C(11)-C(12)	111.3(2)	O(5)-C(17)-O(6)	123.6(3)
C(17)-C(11)-C(12)	110.9(2)	O(5)-C(17)-C(11)	125.5(3)
C(19)-C(11)-C(10)	111.7(2)	O(6)-C(17)-C(11)	110.9(2)
C(17)-C(11)-C(10)	109.3(2)	O(6)-C(18)-H(18A)	109.5
C(12)-C(11)-C(10)	105.5(2)	O(6)-C(18)-H(18B)	109.5
C(8)-C(12)-C(11)	104.5(2)	H(18A)-C(18)-H(18B)	109.5
C(8)-C(12)-H(12A)	110.8	O(6)-C(18)-H(18C)	109.5
C(11)-C(12)-H(12A)	110.8	H(18A)-C(18)-H(18C)	109.5
C(8)-C(12)-H(12B)	110.8	H(18B)-C(18)-H(18C)	109.5
C(11)-C(12)-H(12B)	110.8	O(7)-C(19)-O(8)	123.2(3)
H(12A)-C(12)-H(12B)	108.9	O(7)-C(19)-C(11)	127.1(3)
O(1)-C(13)-O(2)	123.8(3)	O(8)-C(19)-C(11)	109.7(2)
O(1)-C(13)-C(1)	126.0(3)	O(8)-C(20)-H(20A)	109.5
O(2)-C(13)-C(1)	110.2(2)	O(8)-C(20)-H(20B)	109.5
O(2)-C(14)-H(14A)	109.5	H(20A)-C(20)-H(20B)	109.5
O(2)-C(14)-H(14B)	109.5	O(8)-C(20)-H(20C)	109.5
H(14A)-C(14)-H(14B)	109.5	H(20A)-C(20)-H(20C)	109.5
O(2)-C(14)-H(14C)	109.5	H(20B)-C(20)-H(20C)	109.5
H(14A)-C(14)-H(14C)	109.5	C(13)-O(2)-C(14)	115.0(3)
H(14B)-C(14)-H(14C)	109.5	C(15)-O(4)-C(16)	116.2(3)
O(3)-C(15)-O(4)	124.3(3)	C(17)-O(6)-C(18)	115.8(2)
O(3)-C(15)-C(1)	124.4(3)	C(19)-O(8)-C(20)	115.6(2

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for **28a**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	33(1)	23(1)	22(1)	-2(1)	5(1)	-3(1)
C(2)	30(1)	28(2)	22(1)	-2(1)	2(1)	-1(1)
C(3)	40(2)	26(2)	24(2)	0(1)	-2(1)	-2(1)
C(4)	102(3)	32(2)	26(2)	1(1)	-4(2)	-24(2)
C(5)	44(2)	24(2)	24(2)	1(1)	0(1)	-4(1)
C(6)	43(2)	33(2)	21(2)	1(1)	7(1)	0(1)
C(7)	44(2)	27(2)	23(2)	7(1)	6(1)	1(1)
C(8)	43(2)	28(2)	24(2)	1(1)	10(1)	-7(1)
C(9)	149(5)	32(2)	24(2)	9(2)	-17(2)	-36(2)
C(10)	47(2)	21(2)	29(2)	3(1)	1(1)	-5(1)

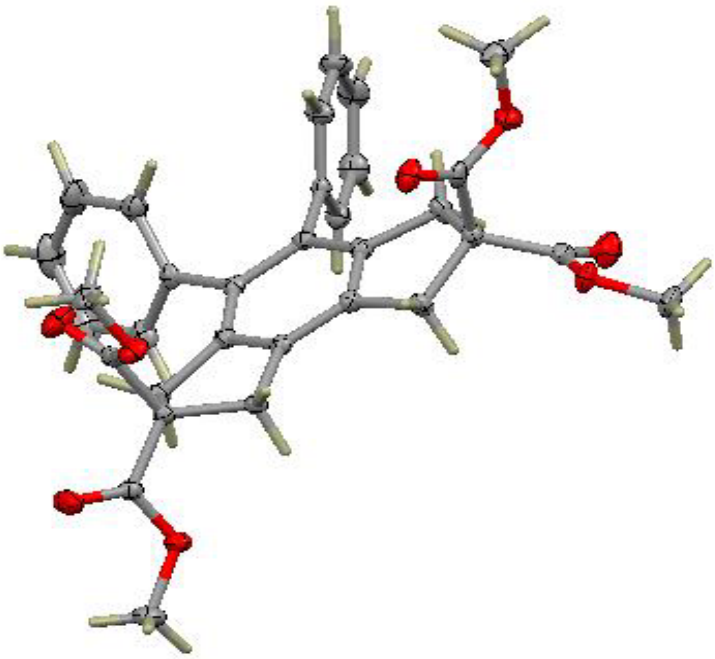
C(11)	28(1)	20(1)	22(1)	3(1)	2(1)	-1(1)
C(12)	33(1)	23(1)	21(1)	3(1)	6(1)	-3(1)
C(13)	32(2)	28(2)	28(2)	-2(1)	9(1)	2(1)
C(14)	49(2)	41(2)	45(2)	4(2)	16(2)	-14(2)
C(15)	27(1)	32(2)	31(2)	7(1)	5(1)	-4(1)
C(16)	37(2)	35(2)	73(3)	-3(2)	23(2)	3(1)
C(17)	22(1)	30(2)	23(1)	1(1)	2(1)	-5(1)
C(18)	39(2)	109(4)	23(2)	-1(2)	8(1)	12(2)
C(19)	27(1)	26(1)	24(1)	0(1)	7(1)	3(1)
C(20)	22(1)	48(2)	49(2)	-14(2)	10(1)	-8(1)
O(1)	33(1)	51(2)	41(1)	6(1)	-1(1)	-11(1)
O(2)	46(1)	38(1)	32(1)	6(1)	3(1)	-14(1)
O(3)	34(1)	64(2)	55(2)	-6(1)	-6(1)	7(1)
O(4)	33(1)	32(1)	47(1)	-11(1)	6(1)	3(1)
O(5)	29(1)	64(2)	28(1)	4(1)	4(1)	14(1)
O(6)	31(1)	61(2)	20(1)	2(1)	3(1)	10(1)
O(7)	30(1)	37(1)	49(1)	6(1)	5(1)	11(1)
O(8)	21(1)	27(1)	44(1)	-8(1)	4(1)	-2(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^{3}) for **28a**.

	x	y	z	U(eq)
H(2A)	9953	6088	5920	32
H(2B)	8112	6239	6301	32
H(5A)	6837	6089	2473	38
H(5B)	8882	5952	2743	38
H(6)	8433	5117	7015	39
H(7)	7211	4262	6039	37
H(10A)	6588	4983	1247	40
H(10B)	4812	5064	1790	40
H(12A)	4912	3938	3634	31
H(12B)	6811	3733	3476	31
H(14A)	10834	7710	3313	66
H(14B)	10206	7586	1762	66
H(14C)	11661	7213	2641	66
H(16A)	4939	7659	4693	70
H(16B)	5608	7663	6270	70
H(16C)	4334	7191	5588	70
H(18A)	8555	4079	-885	85
H(18B)	6930	3868	-1957	85
H(18C)	7838	3474	-784	85
H(20A)	993	3549	966	59
H(20B)	1802	2968	727	59

H(20C)	1673	3433	-381	59

Tetramethyl 4,5-diphenyl-1,3,6,8-tetrahydro-*as*-indacene-2,2,7,7-tetracarboxylate (28b)



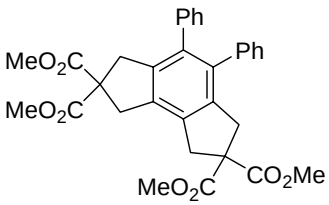


Table 1. Crystal data and structure refinement for **28b**.

Empirical formula	C32 H30 O8	
Formula weight	542.56	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)/c	
Unit cell dimensions	a = 19.6480(10) Å	α= 90°.
	b = 7.6493(3) Å	β= 97.381(2)°.
	c = 18.3142(10) Å	γ = 90°.
Volume	2729.7(2) $Å^3$	
Z	4	
Density (calculated)	1.320 Mg/m^3	
Absorption coefficient	0.095 mm^{-1}	
F(000)	1144	
Crystal size	0.35 x 0.30 x 0.20 mm^3	

Theta range for data collection	1.05 to 26.37°.
Index ranges	-24<=h<=24, -8<=k<=9, -22<=l<=22
Reflections collected	25332
Independent reflections	5503 [R(int) = 0.0389]
Completeness to theta = 26.37°	98.3 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9813 and 0.9676
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5503 / 0 / 481
Goodness-of-fit on F^2	1.172
Final R indices [I>2sigma(I)]	R1 = 0.0393, wR2 = 0.1070
R indices (all data)	R1 = 0.0578, wR2 = 0.1354
Largest diff. peak and hole	0.399 and -0.318 e.$Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **28b**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	1082(1)	1241(2)	4646(1)	15(1)
C(2)	1128(1)	-482(2)	5101(1)	15(1)
C(3)	1849(1)	-397(2)	5496(1)	14(1)
C(4)	2247(1)	798(2)	5161(1)	14(1)
C(5)	1829(1)	1549(2)	4482(1)	15(1)
C(6)	2930(1)	1129(2)	5438(1)	14(1)
C(7)	3228(1)	182(2)	6064(1)	14(1)
C(8)	2824(1)	-1033(2)	6384(1)	15(1)
C(9)	3046(1)	-2250(2)	7021(1)	18(1)
C(10)	2364(1)	-3133(2)	7186(1)	16(1)
C(11)	1827(1)	-2794(2)	6498(1)	18(1)
C(12)	2140(1)	-1338(2)	6103(1)	14(1)
C(13)	887(1)	2787(2)	5111(1)	16(1)
C(14)	177(1)	3814(3)	5951(1)	26(1)
C(15)	581(1)	1170(2)	3942(1)	15(1)
C(16)	256(1)	-394(3)	2848(1)	26(1)
C(17)	2451(1)	-5085(2)	7326(1)	17(1)
C(18)	1852(1)	-7671(2)	7535(1)	25(1)
C(19)	2127(1)	-2295(2)	7871(1)	17(1)
C(20)	2407(1)	-1920(3)	9155(1)	28(1)
C(21)	3326(1)	2507(2)	5097(1)	16(1)
C(22)	3395(1)	2472(2)	4350(1)	22(1)
C(23)	3774(1)	3764(3)	4044(1)	32(1)
C(24)	4085(1)	5090(3)	4478(1)	37(1)

C(25)	4012(1)	5143(3)	5218(1)	33(1)
C(26)	3634(1)	3870(2)	5527(1)	22(1)
C(27)	3973(1)	367(2)	6341(1)	14(1)
C(28)	4198(1)	1117(2)	7021(1)	21(1)
C(29)	4895(1)	1278(3)	7265(1)	27(1)
C(30)	5375(1)	691(3)	6828(1)	28(1)
C(31)	5155(1)	-34(3)	6147(1)	24(1)
C(32)	4461(1)	-197(2)	5903(1)	19(1)
O(1)	1165(1)	4192(2)	5131(1)	30(1)
O(2)	372(1)	2400(2)	5493(1)	21(1)
O(3)	155(1)	2257(2)	3749(1)	29(1)
O(4)	685(1)	-247(2)	3547(1)	21(1)
O(5)	2969(1)	-5907(2)	7317(1)	28(1)
O(6)	1851(1)	-5790(2)	7446(1)	21(1)
O(7)	1637(1)	-1355(2)	7871(1)	26(1)
O(8)	2550(1)	-2732(2)	8474(1)	22(1)

Table 3. Bond lengths [Å] and angles [°] for **28b**.

C(1)-C(15)	1.520(2)	C(11)-H(11B)	0.97(2)
C(1)-C(13)	1.534(2)	C(13)-O(1)	1.203(2)
C(1)-C(5)	1.552(2)	C(13)-O(2)	1.336(2)
C(1)-C(2)	1.556(2)	C(14)-O(2)	1.450(2)
C(2)-C(3)	1.508(2)	C(14)-H(14A)	0.98(2)
C(2)-H(2A)	0.981(19)	C(14)-H(14B)	1.02(2)
C(2)-H(2B)	0.996(19)	C(14)-H(14C)	0.94(3)
C(3)-C(12)	1.385(2)	C(15)-O(3)	1.200(2)
C(3)-C(4)	1.394(2)	C(15)-O(4)	1.333(2)
C(4)-C(6)	1.396(2)	C(16)-O(4)	1.444(2)
C(4)-C(5)	1.513(2)	C(16)-H(16A)	0.96(2)
C(5)-H(5A)	0.99(2)	C(16)-H(16B)	0.95(2)
C(5)-H(5B)	1.04(2)	C(16)-H(16C)	0.99(2)
C(6)-C(7)	1.417(2)	C(17)-O(5)	1.198(2)
C(6)-C(21)	1.494(2)	C(17)-O(6)	1.341(2)
C(7)-C(8)	1.400(2)	C(18)-O(6)	1.448(2)
C(7)-C(27)	1.494(2)	C(18)-H(18A)	0.94(2)
C(8)-C(12)	1.394(2)	C(18)-H(18B)	1.01(2)
C(8)-C(9)	1.512(2)	C(18)-H(18C)	0.96(2)
C(9)-C(10)	1.564(2)	C(19)-O(7)	1.201(2)
C(9)-H(9A)	1.00(2)	C(19)-O(8)	1.338(2)
C(9)-H(9B)	0.98(2)	C(20)-O(8)	1.451(2)
C(10)-C(17)	1.520(2)	C(20)-H(20A)	0.96(2)
C(10)-C(19)	1.532(2)	C(20)-H(20B)	0.99(2)
C(10)-C(11)	1.559(2)	C(20)-H(20C)	0.99(3)
C(11)-C(12)	1.502(2)	C(21)-C(22)	1.393(2)
C(11)-H(11A)	0.99(2)	C(21)-C(26)	1.397(2)

C(22)-C(23)	1.396(3)	C(7)-C(6)-C(21)	120.98(14)
C(22)-H(22)	0.95(2)	C(8)-C(7)-C(6)	118.67(14)
C(23)-C(24)	1.382(3)	C(8)-C(7)-C(27)	120.35(14)
C(23)-H(23)	0.97(2)	C(6)-C(7)-C(27)	120.80(14)
C(24)-C(25)	1.382(3)	C(12)-C(8)-C(7)	121.87(15)
C(24)-H(24)	0.99(2)	C(12)-C(8)-C(9)	110.54(14)
C(25)-C(26)	1.389(3)	C(7)-C(8)-C(9)	127.50(14)
C(25)-H(25)	1.01(3)	C(8)-C(9)-C(10)	104.22(13)
C(26)-H(26)	0.99(2)	C(8)-C(9)-H(9A)	113.0(11)
C(27)-C(28)	1.391(2)	C(10)-C(9)-H(9A)	111.8(11)
C(27)-C(32)	1.394(2)	C(8)-C(9)-H(9B)	111.0(12)
C(28)-C(29)	1.390(3)	C(10)-C(9)-H(9B)	110.1(12)
C(28)-H(28)	0.97(2)	H(9A)-C(9)-H(9B)	106.8(16)
C(29)-C(30)	1.387(3)	C(17)-C(10)-C(19)	108.25(13)
C(29)-H(29)	1.00(2)	C(17)-C(10)-C(11)	110.41(14)
C(30)-C(31)	1.383(3)	C(19)-C(10)-C(11)	110.26(14)
C(30)-H(30)	0.97(2)	C(17)-C(10)-C(9)	112.10(14)
C(31)-C(32)	1.386(2)	C(19)-C(10)-C(9)	109.61(14)
C(31)-H(31)	0.97(2)	C(11)-C(10)-C(9)	106.22(13)
C(32)-H(32)	0.97(2)	C(12)-C(11)-C(10)	103.65(13)
C(15)-C(1)-C(13)	108.50(13)	C(12)-C(11)-H(11A)	112.7(11)
C(15)-C(1)-C(5)	111.51(13)	C(10)-C(11)-H(11A)	111.5(12)
C(13)-C(1)-C(5)	107.42(13)	C(12)-C(11)-H(11B)	110.4(12)
C(15)-C(1)-C(2)	114.23(13)	C(10)-C(11)-H(11B)	111.0(13)
C(13)-C(1)-C(2)	110.95(13)	H(11A)-C(11)-H(11B)	107.6(17)
C(5)-C(1)-C(2)	103.99(12)	C(3)-C(12)-C(8)	119.21(14)
C(3)-C(2)-C(1)	101.90(12)	C(3)-C(12)-C(11)	128.27(14)
C(3)-C(2)-H(2A)	114.0(11)	C(8)-C(12)-C(11)	112.39(14)
C(1)-C(2)-H(2A)	113.1(11)	O(1)-C(13)-O(2)	123.53(15)
C(3)-C(2)-H(2B)	111.1(11)	O(1)-C(13)-C(1)	124.17(15)
C(1)-C(2)-H(2B)	109.6(11)	O(2)-C(13)-C(1)	112.31(13)
H(2A)-C(2)-H(2B)	107.2(15)	O(2)-C(14)-H(14A)	107.2(14)
C(12)-C(3)-C(4)	119.82(14)	O(2)-C(14)-H(14B)	109.5(13)
C(12)-C(3)-C(2)	128.94(14)	H(14A)-C(14)-H(14B)	109.8(18)
C(4)-C(3)-C(2)	111.23(14)	O(2)-C(14)-H(14C)	113.2(14)
C(3)-C(4)-C(6)	121.67(15)	H(14A)-C(14)-H(14C)	111(2)
C(3)-C(4)-C(5)	109.59(14)	H(14B)-C(14)-H(14C)	106(2)
C(6)-C(4)-C(5)	128.71(14)	O(3)-C(15)-O(4)	123.62(15)
C(4)-C(5)-C(1)	102.10(12)	O(3)-C(15)-C(1)	125.20(15)
C(4)-C(5)-H(5A)	115.6(11)	O(4)-C(15)-C(1)	111.16(13)
C(1)-C(5)-H(5A)	110.1(11)	O(4)-C(16)-H(16A)	110.5(13)
C(4)-C(5)-H(5B)	111.0(11)	O(4)-C(16)-H(16B)	107.9(14)
C(1)-C(5)-H(5B)	109.1(11)	H(16A)-C(16)-H(16B)	108.9(18)
H(5A)-C(5)-H(5B)	108.7(15)	O(4)-C(16)-H(16C)	110.7(14)
C(4)-C(6)-C(7)	118.71(14)	H(16A)-C(16)-H(16C)	108.5(18)
C(4)-C(6)-C(21)	120.27(14)	H(16B)-C(16)-H(16C)	110.4(18)

O(5)-C(17)-O(6)	123.89(16)	C(25)-C(24)-H(24)	120.8(14)
O(5)-C(17)-C(10)	126.22(15)	C(24)-C(25)-C(26)	120.5(2)
O(6)-C(17)-C(10)	109.88(13)	C(24)-C(25)-H(25)	121.2(15)
O(6)-C(18)-H(18A)	109.5(14)	C(26)-C(25)-H(25)	118.2(15)
O(6)-C(18)-H(18B)	105.5(13)	C(25)-C(26)-C(21)	120.64(18)
H(18A)-C(18)-H(18B)	110.3(19)	C(25)-C(26)-H(26)	119.4(12)
O(6)-C(18)-H(18C)	109.2(13)	C(21)-C(26)-H(26)	119.9(12)
H(18A)-C(18)-H(18C)	110.3(19)	C(28)-C(27)-C(32)	118.71(15)
H(18B)-C(18)-H(18C)	111.9(17)	C(28)-C(27)-C(7)	121.87(14)
O(7)-C(19)-O(8)	124.18(16)	C(32)-C(27)-C(7)	119.41(15)
O(7)-C(19)-C(10)	125.38(16)	C(29)-C(28)-C(27)	120.74(16)
O(8)-C(19)-C(10)	110.44(13)	C(29)-C(28)-H(28)	122.0(14)
O(8)-C(20)-H(20A)	107.8(14)	C(27)-C(28)-H(28)	117.3(14)
O(8)-C(20)-H(20B)	108.3(12)	C(30)-C(29)-C(28)	120.01(18)
H(20A)-C(20)-H(20B)	110.5(19)	C(30)-C(29)-H(29)	120.4(12)
O(8)-C(20)-H(20C)	106.4(14)	C(28)-C(29)-H(29)	119.5(12)
H(20A)-C(20)-H(20C)	112.5(19)	C(31)-C(30)-C(29)	119.57(17)
H(20B)-C(20)-H(20C)	111.1(19)	C(31)-C(30)-H(30)	118.1(13)
C(22)-C(21)-C(26)	118.57(16)	C(29)-C(30)-H(30)	122.3(13)
C(22)-C(21)-C(6)	121.28(15)	C(30)-C(31)-C(32)	120.49(17)
C(26)-C(21)-C(6)	120.14(15)	C(30)-C(31)-H(31)	121.9(14)
C(21)-C(22)-C(23)	120.30(18)	C(32)-C(31)-H(31)	117.5(14)
C(21)-C(22)-H(22)	119.8(12)	C(31)-C(32)-C(27)	120.47(17)
C(23)-C(22)-H(22)	119.8(12)	C(31)-C(32)-H(32)	119.0(11)
C(24)-C(23)-C(22)	120.54(19)	C(27)-C(32)-H(32)	120.5(11)
C(24)-C(23)-H(23)	122.8(14)	C(13)-O(2)-C(14)	114.36(14)
C(22)-C(23)-H(23)	116.7(14)	C(15)-O(4)-C(16)	115.52(14)
C(23)-C(24)-C(25)	119.49(18)	C(17)-O(6)-C(18)	115.41(14)
C(23)-C(24)-H(24)	119.7(14)	C(19)-O(8)-C(20)	115.73(15)

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for **28b**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	13(1)	15(1)	15(1)	0(1)	0(1)	2(1)
C(2)	13(1)	14(1)	16(1)	0(1)	0(1)	-1(1)
C(3)	13(1)	13(1)	15(1)	-2(1)	2(1)	1(1)
C(4)	15(1)	13(1)	14(1)	-1(1)	2(1)	2(1)
C(5)	14(1)	16(1)	16(1)	2(1)	1(1)	1(1)
C(6)	14(1)	13(1)	14(1)	-2(1)	4(1)	1(1)
C(7)	13(1)	15(1)	13(1)	-3(1)	2(1)	0(1)
C(8)	15(1)	15(1)	15(1)	1(1)	2(1)	1(1)
C(9)	14(1)	22(1)	19(1)	7(1)	0(1)	-1(1)
C(10)	15(1)	16(1)	18(1)	3(1)	1(1)	0(1)

C(11)	15(1)	19(1)	19(1)	5(1)	-1(1)	-1(1)
C(12)	14(1)	14(1)	15(1)	0(1)	3(1)	0(1)
C(13)	14(1)	17(1)	16(1)	0(1)	-3(1)	2(1)
C(14)	35(1)	22(1)	22(1)	-6(1)	9(1)	6(1)
C(15)	14(1)	16(1)	16(1)	-1(1)	1(1)	-1(1)
C(16)	31(1)	29(1)	18(1)	-5(1)	-4(1)	-3(1)
C(17)	18(1)	18(1)	14(1)	1(1)	2(1)	0(1)
C(18)	31(1)	11(1)	33(1)	0(1)	4(1)	-1(1)
C(19)	18(1)	10(1)	24(1)	3(1)	4(1)	-4(1)
C(20)	39(1)	25(1)	22(1)	-5(1)	10(1)	-10(1)
C(21)	11(1)	15(1)	21(1)	4(1)	2(1)	3(1)
C(22)	20(1)	25(1)	21(1)	4(1)	6(1)	7(1)
C(23)	28(1)	40(1)	33(1)	17(1)	16(1)	9(1)
C(24)	25(1)	33(1)	54(1)	23(1)	11(1)	-3(1)
C(25)	25(1)	22(1)	50(1)	8(1)	-2(1)	-7(1)
C(26)	20(1)	19(1)	28(1)	3(1)	-2(1)	-1(1)
C(27)	14(1)	12(1)	17(1)	2(1)	2(1)	-1(1)
C(28)	19(1)	24(1)	21(1)	-2(1)	1(1)	3(1)
C(29)	22(1)	30(1)	28(1)	-6(1)	-8(1)	-1(1)
C(30)	12(1)	28(1)	40(1)	2(1)	-4(1)	-2(1)
C(31)	17(1)	26(1)	32(1)	3(1)	8(1)	3(1)
C(32)	18(1)	17(1)	21(1)	0(1)	4(1)	1(1)
O(1)	34(1)	19(1)	37(1)	-9(1)	11(1)	-5(1)
O(2)	22(1)	19(1)	24(1)	-6(1)	7(1)	2(1)
O(3)	31(1)	28(1)	26(1)	-6(1)	-10(1)	13(1)
O(4)	24(1)	20(1)	17(1)	-5(1)	-3(1)	2(1)
O(5)	22(1)	21(1)	44(1)	2(1)	7(1)	5(1)
O(6)	21(1)	11(1)	32(1)	3(1)	7(1)	0(1)
O(7)	27(1)	18(1)	36(1)	1(1)	9(1)	5(1)
O(8)	26(1)	22(1)	18(1)	-1(1)	3(1)	0(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3) for **28b**.

	x	y	z	U(eq)
H(2A)	773(10)	-570(20)	5430(10)	17(5)
H(2B)	1069(9)	-1500(20)	4761(10)	14(4)
H(5A)	1903(9)	2810(30)	4391(10)	18(5)
H(5B)	1908(10)	850(20)	4015(11)	19(5)
H(9A)	3285(10)	-1630(30)	7465(11)	19(5)
H(9B)	3366(10)	-3140(30)	6883(11)	24(5)
H(11A)	1375(11)	-2480(30)	6640(11)	21(5)
H(11B)	1766(11)	-3830(30)	6188(12)	24(5)
H(14A)	-230(12)	3430(30)	6163(13)	38(6)
H(14B)	569(12)	4060(30)	6362(13)	36(6)

H(14C)	92(12)	4870(30)	5693(13)	41(7)
H(16A)	-217(12)	-510(30)	2921(11)	27(5)
H(16B)	391(11)	-1410(30)	2608(12)	32(6)
H(16C)	304(12)	650(30)	2541(13)	36(6)
H(18A)	1917(11)	-8210(30)	7087(13)	34(6)
H(18B)	1385(12)	-7970(30)	7672(12)	33(6)
H(18C)	2215(11)	-8000(30)	7915(12)	28(5)
H(20A)	1924(13)	-2070(30)	9188(12)	37(6)
H(20B)	2524(11)	-660(30)	9136(11)	28(5)
H(20C)	2701(12)	-2520(30)	9557(14)	37(6)
H(22)	3195(11)	1550(30)	4049(12)	25(5)
H(23)	3809(12)	3670(30)	3522(14)	39(6)
H(24)	4351(12)	5990(30)	4255(13)	38(6)
H(25)	4253(13)	6060(30)	5555(14)	51(7)
H(26)	3593(10)	3920(30)	6058(12)	23(5)
H(28)	3849(12)	1510(30)	7315(12)	36(6)
H(29)	5047(11)	1840(30)	7755(13)	32(6)
H(30)	5867(12)	760(30)	6986(12)	32(6)
H(31)	5474(11)	-490(30)	5833(12)	33(6)
H(32)	4319(9)	-680(20)	5415(11)	15(4)

Tetramethyl 4,5-diphenyl-1,3,4,6,8,8a-hexahydro-*as*-indacene-2,2,7,7-tetracarboxylate (29b)

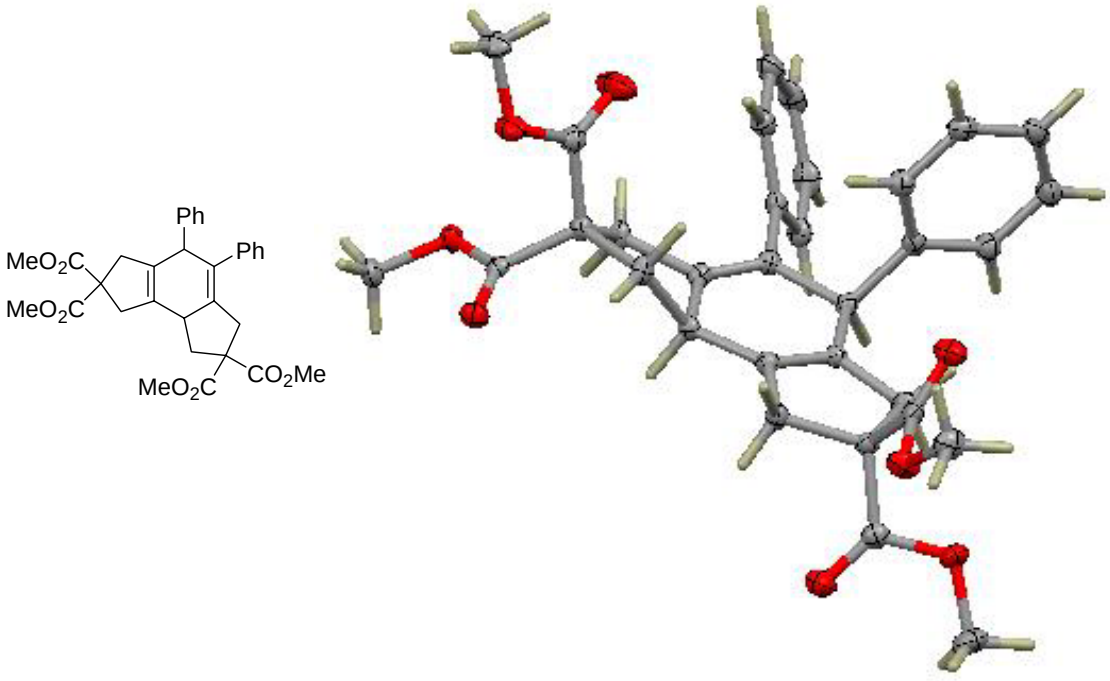


Table 1. Crystal data and structure refinement for **29b**.

Empirical formula	C32 H32 O8	
Formula weight	544.58	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)/c	
Unit cell dimensions	a = 8.6108(6) Å	α= 90°.
	b = 11.1917(8) Å	β= 97.657(4)°.
	c = 28.338(2) Å	γ = 90°.
Volume	2706.6(3) $Å^3$	
Z	4	
Density (calculated)	1.336 Mg/m^3	
Absorption coefficient	0.096 mm^{-1}	
F(000)	1152	
Crystal size	0.35 x 0.15 x 0.10 mm^3	
Theta range for data collection	1.45 to 28.36°.	
Index ranges	-10<=h<=11, -14<=k<=14, -37<=l<=37	
Reflections collected	83819	
Independent reflections	6756 [R(int) = 0.0602]	
Completeness to theta = 28.36°	99.7 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9905 and 0.9673	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6756 / 0 / 489	
Goodness-of-fit on F^2	1.030	
Final R indices [I>2sigma(I)]	R1 = 0.0390, wR2 = 0.0962	
R indices (all data)	R1 = 0.0532, wR2 = 0.1079	
Largest diff. peak and hole	0.484 and -0.227 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **29b**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	9404(1)	7977(1)	966(1)	16(1)
C(2)	7945(1)	7267(1)	727(1)	18(1)
C(3)	7383(1)	6601(1)	1134(1)	15(1)

C(4)	8258(1)	6822(1)	1549(1)	14(1)
C(5)	9561(1)	7686(1)	1509(1)	18(1)
C(6)	8035(1)	6264(1)	2017(1)	14(1)
C(7)	6632(1)	5430(1)	1973(1)	14(1)
C(8)	5692(1)	5298(1)	1563(1)	14(1)
C(9)	5923(1)	5875(1)	1096(1)	14(1)
C(10)	5740(1)	4788(1)	759(1)	17(1)
C(11)	4367(1)	4073(1)	928(1)	14(1)
C(12)	4312(1)	4472(1)	1454(1)	16(1)
C(13)	9202(1)	9319(1)	887(1)	18(1)
C(14)	10440(2)	11175(1)	1053(1)	33(1)
C(15)	10877(1)	7573(1)	765(1)	16(1)
C(16)	12478(2)	7896(1)	164(1)	25(1)
C(17)	9527(1)	5592(1)	2213(1)	15(1)
C(18)	9972(2)	4591(1)	1971(1)	19(1)
C(19)	11344(2)	3988(1)	2134(1)	21(1)
C(20)	12294(2)	4378(1)	2539(1)	24(1)
C(21)	11862(2)	5367(1)	2782(1)	24(1)
C(22)	10479(2)	5972(1)	2620(1)	20(1)
C(23)	6410(1)	4760(1)	2415(1)	16(1)
C(24)	6532(1)	3518(1)	2434(1)	19(1)
C(25)	6334(2)	2898(1)	2848(1)	24(1)
C(26)	6011(2)	3519(1)	3246(1)	26(1)
C(27)	5908(2)	4751(1)	3235(1)	25(1)
C(28)	6115(1)	5373(1)	2822(1)	19(1)
C(29)	2813(1)	4326(1)	618(1)	14(1)
C(30)	87(2)	4084(1)	577(1)	23(1)
C(31)	4700(1)	2738(1)	904(1)	18(1)
C(32)	4242(2)	990(1)	440(1)	24(1)
O(1)	8078(1)	9808(1)	676(1)	27(1)
O(2)	10470(1)	9892(1)	1098(1)	26(1)
O(3)	11769(1)	6821(1)	937(1)	24(1)
O(4)	11041(1)	8152(1)	360(1)	23(1)
O(5)	2638(1)	4844(1)	243(1)	20(1)
O(6)	1631(1)	3871(1)	826(1)	18(1)
O(7)	5455(2)	2176(1)	1212(1)	45(1)
O(8)	4068(1)	2269(1)	492(1)	24(1)

Table 3. Bond lengths [Å] and angles [°] for **29b**.

C(1)-C(13)	1.5244(17)	C(2)-H(2B)	1.001(18)
C(1)-C(15)	1.5267(17)	C(3)-C(4)	1.3311(17)
C(1)-C(5)	1.5607(17)	C(3)-C(9)	1.4886(16)
C(1)-C(2)	1.5626(16)	C(4)-C(5)	1.4972(16)
C(2)-C(3)	1.5063(16)	C(4)-C(6)	1.5027(16)
C(2)-H(2A)	0.968(16)	C(5)-H(5A)	0.978(18)

C(5)-H(5B)	0.988(15)	C(25)-H(25)	0.982(18)
C(6)-C(7)	1.5188(16)	C(26)-C(27)	1.382(2)
C(6)-C(17)	1.5278(16)	C(26)-H(26)	0.964(19)
C(6)-H(6)	0.999(16)	C(27)-C(28)	1.3925(18)
C(7)-C(8)	1.3315(16)	C(27)-H(27)	0.951(19)
C(7)-C(23)	1.4934(16)	C(28)-H(28)	0.962(16)
C(8)-C(12)	1.5054(16)	C(29)-O(5)	1.2016(15)
C(8)-C(9)	1.5103(16)	C(29)-O(6)	1.3429(14)
C(9)-C(10)	1.5425(17)	C(30)-O(6)	1.4399(15)
C(9)-H(9)	1.014(15)	C(30)-H(30A)	0.971(19)
C(10)-C(11)	1.5551(16)	C(30)-H(30B)	0.97(2)
C(10)-H(10A)	0.979(17)	C(30)-H(30C)	0.953(19)
C(10)-H(10B)	1.008(16)	C(31)-O(7)	1.1937(16)
C(11)-C(31)	1.5246(17)	C(31)-O(8)	1.3310(15)
C(11)-C(29)	1.5258(16)	C(32)-O(8)	1.4481(16)
C(11)-C(12)	1.5632(16)	C(32)-H(32A)	0.953(19)
C(12)-H(12A)	0.968(16)	C(32)-H(32B)	0.999(18)
C(12)-H(12B)	0.974(16)	C(32)-H(32C)	0.971(18)
C(13)-O(1)	1.2006(16)	C(13)-C(1)-C(15)	108.70(10)
C(13)-O(2)	1.3369(15)	C(13)-C(1)-C(5)	110.13(10)
C(14)-O(2)	1.4417(17)	C(15)-C(1)-C(5)	109.83(10)
C(14)-H(14A)	0.979(19)	C(13)-C(1)-C(2)	111.56(10)
C(14)-H(14B)	0.98(2)	C(15)-C(1)-C(2)	110.34(10)
C(14)-H(14C)	0.954(19)	C(5)-C(1)-C(2)	106.27(9)
C(15)-O(3)	1.1988(15)	C(3)-C(2)-C(1)	103.99(10)
C(15)-O(4)	1.3425(15)	C(3)-C(2)-H(2A)	112.8(9)
C(16)-O(4)	1.4507(16)	C(1)-C(2)-H(2A)	109.0(9)
C(16)-H(16A)	0.983(18)	C(3)-C(2)-H(2B)	111.8(10)
C(16)-H(16B)	0.948(18)	C(1)-C(2)-H(2B)	112.1(9)
C(16)-H(16C)	0.984(16)	H(2A)-C(2)-H(2B)	107.3(13)
C(17)-C(22)	1.3881(17)	C(4)-C(3)-C(9)	122.62(11)
C(17)-C(18)	1.3925(18)	C(4)-C(3)-C(2)	112.45(10)
C(18)-C(19)	1.3857(18)	C(9)-C(3)-C(2)	124.63(10)
C(18)-H(18)	0.973(17)	C(3)-C(4)-C(5)	113.31(11)
C(19)-C(20)	1.386(2)	C(3)-C(4)-C(6)	125.36(11)
C(19)-H(19)	0.985(17)	C(5)-C(4)-C(6)	121.32(10)
C(20)-C(21)	1.381(2)	C(4)-C(5)-C(1)	103.96(9)
C(20)-H(20)	0.972(18)	C(4)-C(5)-H(5A)	112.0(10)
C(21)-C(22)	1.3947(18)	C(1)-C(5)-H(5A)	111.1(10)
C(21)-H(21)	0.954(15)	C(4)-C(5)-H(5B)	112.4(9)
C(22)-H(22)	0.956(15)	C(1)-C(5)-H(5B)	110.5(9)
C(23)-C(28)	1.3948(17)	H(5A)-C(5)-H(5B)	106.9(13)
C(23)-C(24)	1.3953(18)	C(4)-C(6)-C(7)	112.06(9)
C(24)-C(25)	1.3909(18)	C(4)-C(6)-C(17)	109.00(9)
C(24)-H(24)	0.954(17)	C(7)-C(6)-C(17)	110.42(10)
C(25)-C(26)	1.386(2)	C(4)-C(6)-H(6)	108.9(9)

C(7)-C(6)-H(6)	108.8(9)	H(16A)-C(16)-H(16B)	111.0(14)
C(17)-C(6)-H(6)	107.6(8)	O(4)-C(16)-H(16C)	109.6(9)
C(8)-C(7)-C(23)	122.99(11)	H(16A)-C(16)-H(16C)	109.6(13)
C(8)-C(7)-C(6)	121.66(11)	H(16B)-C(16)-H(16C)	111.7(14)
C(23)-C(7)-C(6)	115.33(10)	C(22)-C(17)-C(18)	118.94(11)
C(7)-C(8)-C(12)	128.26(11)	C(22)-C(17)-C(6)	121.67(11)
C(7)-C(8)-C(9)	125.54(11)	C(18)-C(17)-C(6)	119.36(11)
C(12)-C(8)-C(9)	105.92(9)	C(19)-C(18)-C(17)	120.42(12)
C(3)-C(9)-C(8)	112.19(10)	C(19)-C(18)-H(18)	120.9(10)
C(3)-C(9)-C(10)	119.41(10)	C(17)-C(18)-H(18)	118.7(10)
C(8)-C(9)-C(10)	101.02(9)	C(18)-C(19)-C(20)	120.31(13)
C(3)-C(9)-H(9)	108.3(8)	C(18)-C(19)-H(19)	118.8(9)
C(8)-C(9)-H(9)	109.0(9)	C(20)-C(19)-H(19)	120.9(9)
C(10)-C(9)-H(9)	106.4(8)	C(21)-C(20)-C(19)	119.81(12)
C(9)-C(10)-C(11)	103.57(9)	C(21)-C(20)-H(20)	119.5(10)
C(9)-C(10)-H(10A)	113.9(10)	C(19)-C(20)-H(20)	120.7(10)
C(11)-C(10)-H(10A)	112.1(10)	C(20)-C(21)-C(22)	119.91(12)
C(9)-C(10)-H(10B)	109.2(9)	C(20)-C(21)-H(21)	120.4(9)
C(11)-C(10)-H(10B)	108.6(9)	C(22)-C(21)-H(21)	119.7(9)
H(10A)-C(10)-H(10B)	109.3(13)	C(17)-C(22)-C(21)	120.61(12)
C(31)-C(11)-C(29)	108.24(9)	C(17)-C(22)-H(22)	118.9(9)
C(31)-C(11)-C(10)	109.61(10)	C(21)-C(22)-H(22)	120.4(9)
C(29)-C(11)-C(10)	111.86(10)	C(28)-C(23)-C(24)	118.56(11)
C(31)-C(11)-C(12)	110.54(10)	C(28)-C(23)-C(7)	120.33(11)
C(29)-C(11)-C(12)	111.09(9)	C(24)-C(23)-C(7)	121.08(11)
C(10)-C(11)-C(12)	105.50(9)	C(25)-C(24)-C(23)	120.85(12)
C(8)-C(12)-C(11)	104.41(9)	C(25)-C(24)-H(24)	119.0(10)
C(8)-C(12)-H(12A)	109.0(9)	C(23)-C(24)-H(24)	120.1(10)
C(11)-C(12)-H(12A)	108.8(9)	C(26)-C(25)-C(24)	119.86(13)
C(8)-C(12)-H(12B)	114.7(9)	C(26)-C(25)-H(25)	121.4(10)
C(11)-C(12)-H(12B)	111.0(9)	C(24)-C(25)-H(25)	118.7(10)
H(12A)-C(12)-H(12B)	108.8(13)	C(27)-C(26)-C(25)	119.99(12)
O(1)-C(13)-O(2)	124.05(12)	C(27)-C(26)-H(26)	119.7(11)
O(1)-C(13)-C(1)	126.28(12)	C(25)-C(26)-H(26)	120.3(11)
O(2)-C(13)-C(1)	109.66(10)	C(26)-C(27)-C(28)	120.21(13)
O(2)-C(14)-H(14A)	108.2(11)	C(26)-C(27)-H(27)	122.3(11)
O(2)-C(14)-H(14B)	104.3(11)	C(28)-C(27)-H(27)	117.4(11)
H(14A)-C(14)-H(14B)	113.0(16)	C(27)-C(28)-C(23)	120.52(13)
O(2)-C(14)-H(14C)	109.9(11)	C(27)-C(28)-H(28)	119.7(9)
H(14A)-C(14)-H(14C)	110.9(15)	C(23)-C(28)-H(28)	119.7(9)
H(14B)-C(14)-H(14C)	110.4(16)	O(5)-C(29)-O(6)	123.97(11)
O(3)-C(15)-O(4)	123.53(12)	O(5)-C(29)-C(11)	126.48(11)
O(3)-C(15)-C(1)	125.10(11)	O(6)-C(29)-C(11)	109.54(10)
O(4)-C(15)-C(1)	111.35(10)	O(6)-C(30)-H(30A)	105.2(10)
O(4)-C(16)-H(16A)	111.3(10)	O(6)-C(30)-H(30B)	111.3(11)
O(4)-C(16)-H(16B)	103.5(10)	H(30A)-C(30)-H(30B)	107.9(15)

O(6)-C(30)-H(30C)	109.4(11)	H(32A)-C(32)-H(32B)	110.0(15)
H(30A)-C(30)-H(30C)	111.1(15)	O(8)-C(32)-H(32C)	110.9(10)
H(30B)-C(30)-H(30C)	111.8(16)	H(32A)-C(32)-H(32C)	112.3(15)
O(7)-C(31)-O(8)	123.57(12)	H(32B)-C(32)-H(32C)	109.6(14)
O(7)-C(31)-C(11)	124.89(12)	C(13)-O(2)-C(14)	115.79(11)
O(8)-C(31)-C(11)	111.53(10)	C(15)-O(4)-C(16)	115.16(10)
O(8)-C(32)-H(32A)	105.5(11)	C(29)-O(6)-C(30)	115.17(10)
O(8)-C(32)-H(32B)	108.5(10)	C(31)-O(8)-C(32)	116.26(10)

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for **29b**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	18(1)	15(1)	16(1)	1(1)	1(1)	-2(1)
C(2)	18(1)	20(1)	15(1)	3(1)	1(1)	-4(1)
C(3)	15(1)	15(1)	15(1)	1(1)	2(1)	0(1)
C(4)	15(1)	13(1)	15(1)	0(1)	2(1)	0(1)
C(5)	20(1)	19(1)	14(1)	2(1)	1(1)	-5(1)
C(6)	16(1)	15(1)	12(1)	-1(1)	1(1)	-1(1)
C(7)	15(1)	15(1)	14(1)	0(1)	4(1)	0(1)
C(8)	15(1)	15(1)	14(1)	-1(1)	5(1)	-1(1)
C(9)	14(1)	17(1)	12(1)	1(1)	2(1)	-1(1)
C(10)	16(1)	22(1)	14(1)	-2(1)	4(1)	-4(1)
C(11)	14(1)	17(1)	12(1)	0(1)	2(1)	-1(1)
C(12)	16(1)	21(1)	12(1)	-2(1)	3(1)	-4(1)
C(13)	20(1)	18(1)	18(1)	1(1)	5(1)	-1(1)
C(14)	41(1)	15(1)	41(1)	2(1)	2(1)	-4(1)
C(15)	19(1)	14(1)	16(1)	0(1)	0(1)	-4(1)
C(16)	22(1)	27(1)	27(1)	4(1)	10(1)	-1(1)
C(17)	15(1)	17(1)	15(1)	4(1)	3(1)	-2(1)
C(18)	19(1)	21(1)	17(1)	1(1)	4(1)	-1(1)
C(19)	20(1)	19(1)	26(1)	4(1)	9(1)	1(1)
C(20)	15(1)	25(1)	30(1)	11(1)	3(1)	0(1)
C(21)	21(1)	28(1)	23(1)	4(1)	-4(1)	-3(1)
C(22)	21(1)	21(1)	18(1)	0(1)	1(1)	-1(1)
C(23)	12(1)	22(1)	13(1)	2(1)	1(1)	-1(1)
C(24)	17(1)	22(1)	19(1)	1(1)	2(1)	0(1)
C(25)	20(1)	26(1)	26(1)	9(1)	1(1)	1(1)
C(26)	21(1)	39(1)	17(1)	12(1)	1(1)	-2(1)
C(27)	23(1)	39(1)	12(1)	-1(1)	2(1)	-2(1)
C(28)	19(1)	24(1)	15(1)	-1(1)	2(1)	-2(1)
C(29)	17(1)	12(1)	13(1)	-2(1)	3(1)	-1(1)
C(30)	14(1)	24(1)	28(1)	3(1)	-2(1)	0(1)
C(31)	19(1)	19(1)	18(1)	0(1)	2(1)	-1(1)

C(32)	34(1)	18(1)	22(1)	-4(1)	3(1)	5(1)
O(1)	25(1)	22(1)	34(1)	5(1)	1(1)	4(1)
O(2)	28(1)	14(1)	34(1)	3(1)	-3(1)	-4(1)
O(3)	28(1)	21(1)	22(1)	2(1)	3(1)	6(1)
O(4)	22(1)	26(1)	24(1)	8(1)	9(1)	3(1)
O(5)	23(1)	21(1)	16(1)	3(1)	3(1)	1(1)
O(6)	13(1)	21(1)	19(1)	3(1)	2(1)	-2(1)
O(7)	68(1)	25(1)	34(1)	-2(1)	-22(1)	13(1)
O(8)	33(1)	18(1)	19(1)	-4(1)	-2(1)	5(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3) for **29b**.

	x	y	z	U(eq)
H(2A)	7176(19)	7827(14)	577(6)	22(4)
H(2B)	8216(19)	6711(15)	474(6)	27(4)
H(5A)	9460(20)	8410(16)	1697(6)	30(4)
H(5B)	10602(18)	7342(14)	1620(5)	19(4)
H(6)	7875(17)	6912(14)	2249(5)	17(4)
H(9)	5000(17)	6420(13)	991(5)	17(3)
H(10A)	5530(19)	4999(15)	421(6)	24(4)
H(10B)	6718(18)	4285(14)	815(5)	20(4)
H(12A)	3357(18)	4919(14)	1468(6)	21(4)
H(12B)	4321(18)	3783(15)	1664(6)	22(4)
H(14A)	10450(20)	11377(16)	717(7)	35(5)
H(14B)	11390(20)	11440(17)	1257(7)	41(5)
H(14C)	9530(20)	11487(17)	1167(7)	35(5)
H(16A)	12585(19)	7037(16)	104(6)	26(4)
H(16B)	12363(19)	8334(15)	-125(6)	27(4)
H(16C)	13382(19)	8175(14)	385(6)	23(4)
H(18)	9310(20)	4334(15)	1684(6)	27(4)
H(19)	11628(19)	3279(15)	1958(6)	25(4)
H(20)	13250(20)	3953(16)	2657(6)	31(4)
H(21)	12505(17)	5639(13)	3062(5)	17(4)
H(22)	10176(17)	6662(14)	2784(5)	16(4)
H(24)	6742(18)	3079(15)	2161(6)	24(4)
H(25)	6439(19)	2025(16)	2850(6)	28(4)
H(26)	5850(20)	3094(17)	3531(7)	37(5)
H(27)	5650(20)	5204(16)	3497(7)	33(5)
H(28)	6023(18)	6229(15)	2815(6)	21(4)
H(30A)	-610(20)	3629(16)	749(6)	32(4)
H(30B)	-10(20)	3776(18)	253(7)	44(5)
H(30C)	-140(20)	4917(17)	583(6)	34(5)
H(32A)	3870(20)	822(16)	115(7)	37(5)
H(32B)	3570(20)	580(16)	652(6)	29(4)

H(32C)	5330(20)	750(16)	527(6)	30(4)

(*E*)-Dimethyl 3-ethylidene-4-((*E*)-7-ethylidene-5-(methoxycarbonyl)-4-oxo-2-phenyl-3-oxa-bicyclo[3.2.1]octan-1-yl)cyclopentane-1,1-dicarboxylate (37a)

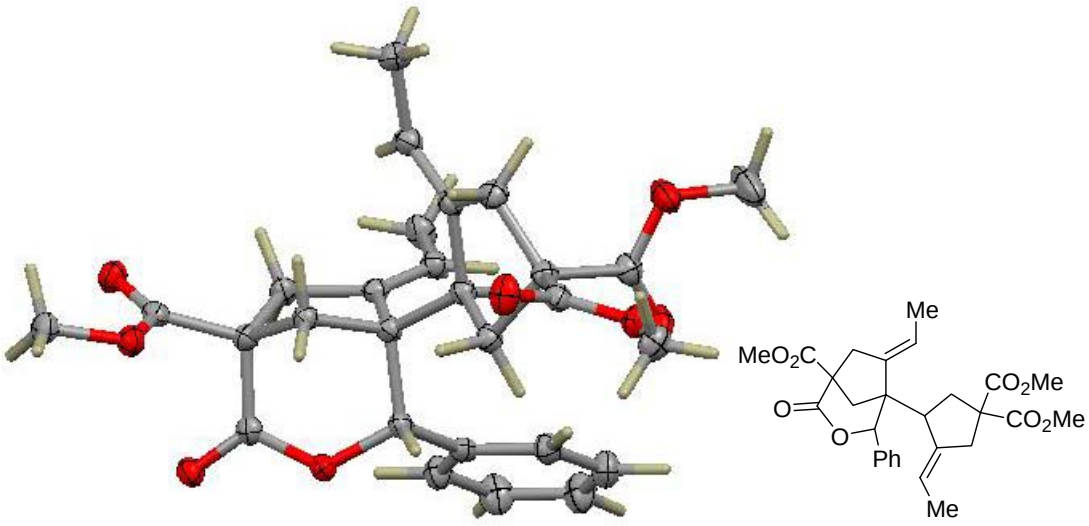


Table 1. Crystal data and structure refinement for **37a**.

Empirical formula	C28 H32 O8	
Formula weight	496.54	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P2(1)/c	
Unit cell dimensions	a = 10.3811(2) Å	α= 90°.
	b = 9.15330(10) Å	β= 91.9380(10)°.
	c = 26.1805(4) Å	γ = 90°.
Volume	2486.28(7) $Å^3$	
Z	4	
Density (calculated)	1.327 Mg/m^3	
Absorption coefficient	0.800 mm^{-1}	
F(000)	1056	
Crystal size	0.20 x 0.20 x 0.10 mm^3	
Theta range for data collection	3.38 to 71.97°.	
Index ranges	-12<=h<=12, -11<=k<=10, -30<=l<=32	

Reflections collected	23952
Independent reflections	4781 [R(int) = 0.0258]
Completeness to theta = 71.97°	98.0 %
Absorption correction	Semi-empirical from equivalents
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4781 / 0 / 453
Goodness-of-fit on F^2	1.033
Final R indices [I>2sigma(I)]	R1 = 0.0335, wR2 = 0.0881
R indices (all data)	R1 = 0.0354, wR2 = 0.0900
Largest diff. peak and hole	0.311 and -0.190 e.Å^{-3}

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for **37a**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	5115(1)	10843(1)	8761(1)	20(1)
C(2)	4367(1)	9778(1)	9097(1)	22(1)
C(3)	5262(1)	8476(1)	9174(1)	19(1)
C(4)	6597(1)	8895(1)	8982(1)	18(1)
C(5)	6516(1)	10579(1)	8954(1)	19(1)
C(6)	4979(1)	10478(1)	8191(1)	22(1)
C(7)	3494(2)	9904(2)	7521(1)	46(1)
C(8)	4698(1)	12423(1)	8845(1)	21(1)
C(9)	4139(1)	14660(1)	8445(1)	27(1)
C(10)	4914(1)	7242(1)	9398(1)	22(1)
C(11)	3610(1)	6947(1)	9605(1)	26(1)
C(12)	7760(1)	8265(1)	9292(1)	18(1)
C(13)	7678(1)	8477(1)	9872(1)	18(1)
C(14)	8713(1)	7394(1)	10067(1)	18(1)
C(15)	8482(1)	6018(1)	9733(1)	21(1)
C(16)	7930(1)	6617(1)	9233(1)	18(1)
C(17)	7702(1)	5856(1)	8809(1)	20(1)
C(18)	7952(1)	4256(1)	8743(1)	25(1)
C(19)	8702(1)	7064(1)	10635(1)	19(1)
C(20)	8715(1)	8123(2)	11454(1)	25(1)
C(21)	10015(1)	8042(1)	9952(1)	18(1)
C(22)	9045(1)	9019(1)	9136(1)	18(1)
C(23)	9551(1)	8530(1)	8627(1)	19(1)
C(24)	9024(1)	9094(1)	8171(1)	23(1)
C(25)	9468(1)	8631(1)	7704(1)	28(1)
C(26)	10452(1)	7613(2)	7684(1)	32(1)
C(27)	10982(1)	7050(2)	8137(1)	32(1)
C(28)	10533(1)	7497(1)	8603(1)	25(1)

O(1)	5845(1)	10482(1)	7897(1)	28(1)
O(2)	3755(1)	10164(1)	8058(1)	30(1)
O(3)	4530(1)	12952(1)	9257(1)	29(1)
O(4)	4549(1)	13149(1)	8402(1)	23(1)
O(5)	8755(1)	5863(1)	10820(1)	25(1)
O(6)	8630(1)	8300(1)	10906(1)	23(1)
O(7)	10104(1)	8796(1)	9515(1)	20(1)
O(8)	10967(1)	7914(1)	10227(1)	22(1)

Table 3. Bond lengths [Å] and angles [°] for **37a**.

C(1)-C(8)	1.5283(15)	C(13)-C(14)	1.5365(15)
C(1)-C(6)	1.5322(15)	C(13)-H(13A)	0.974(15)
C(1)-C(2)	1.5397(16)	C(13)-H(13B)	0.981(14)
C(1)-C(5)	1.5416(15)	C(14)-C(21)	1.5148(15)
C(2)-C(3)	1.5201(16)	C(14)-C(19)	1.5186(15)
C(2)-H(2A)	0.989(16)	C(14)-C(15)	1.5474(15)
C(2)-H(2B)	0.973(16)	C(15)-C(16)	1.5137(15)
C(3)-C(10)	1.3277(17)	C(15)-H(15A)	0.975(16)
C(3)-C(4)	1.5394(15)	C(15)-H(15B)	1.006(16)
C(4)-C(12)	1.5434(15)	C(16)-C(17)	1.3257(16)
C(4)-C(5)	1.5455(15)	C(17)-C(18)	1.4984(16)
C(4)-H(4)	0.973(13)	C(17)-H(17)	0.996(15)
C(5)-H(5A)	0.996(15)	C(18)-H(17A)	0.994(18)
C(5)-H(5B)	0.991(14)	C(18)-H(17B)	0.99(2)
C(6)-O(1)	1.2031(15)	C(18)-H(17C)	0.959(18)
C(6)-O(2)	1.3371(15)	C(19)-O(5)	1.2021(14)
C(7)-O(2)	1.4432(16)	C(19)-O(6)	1.3387(14)
C(7)-H(7A)	0.98(2)	C(20)-O(6)	1.4416(14)
C(7)-H(7B)	1.02(2)	C(20)-H(20A)	0.967(18)
C(7)-H(7C)	1.00(2)	C(20)-H(20B)	0.962(18)
C(8)-O(3)	1.1988(14)	C(20)-H(20C)	0.968(16)
C(8)-O(4)	1.3410(14)	C(21)-O(8)	1.2083(14)
C(9)-O(4)	1.4522(14)	C(21)-O(7)	1.3423(13)
C(9)-H(9A)	0.957(16)	C(22)-O(7)	1.4711(12)
C(9)-H(9B)	0.977(17)	C(22)-C(23)	1.5142(15)
C(9)-H(9C)	0.971(17)	C(22)-H(22)	0.973(14)
C(10)-C(11)	1.5001(16)	C(23)-C(28)	1.3935(16)
C(10)-H(10)	0.985(15)	C(23)-C(24)	1.3954(16)
C(11)-H(11A)	0.971(17)	C(24)-C(25)	1.3889(17)
C(11)-H(11B)	0.986(19)	C(24)-H(24)	0.973(16)
C(11)-H(11C)	0.980(18)	C(25)-C(26)	1.3849(19)
C(12)-C(16)	1.5277(15)	C(25)-H(25)	0.977(17)
C(12)-C(13)	1.5378(15)	C(26)-C(27)	1.3877(19)
C(12)-C(22)	1.5674(15)	C(26)-H(26)	0.967(18)

C(27)-C(28)	1.3836(18)	H(9A)-C(9)-H(9C)	111.1(13)
C(27)-H(27)	0.975(18)	H(9B)-C(9)-H(9C)	110.7(13)
C(28)-H(28)	0.979(15)	C(3)-C(10)-C(11)	125.10(11)
C(8)-C(1)-C(6)	109.25(9)	C(3)-C(10)-H(10)	119.4(9)
C(8)-C(1)-C(2)	111.47(9)	C(11)-C(10)-H(10)	115.5(9)
C(6)-C(1)-C(2)	112.70(9)	C(10)-C(11)-H(11A)	110.2(10)
C(8)-C(1)-C(5)	111.69(9)	C(10)-C(11)-H(11B)	112.2(10)
C(6)-C(1)-C(5)	109.87(9)	H(11A)-C(11)-H(11B)	107.1(14)
C(2)-C(1)-C(5)	101.71(9)	C(10)-C(11)-H(11C)	111.5(10)
C(3)-C(2)-C(1)	104.76(9)	H(11A)-C(11)-H(11C)	106.8(14)
C(3)-C(2)-H(2A)	114.1(9)	H(11B)-C(11)-H(11C)	108.7(14)
C(1)-C(2)-H(2A)	113.3(9)	C(16)-C(12)-C(13)	103.54(8)
C(3)-C(2)-H(2B)	110.4(9)	C(16)-C(12)-C(4)	114.02(9)
C(1)-C(2)-H(2B)	107.0(9)	C(13)-C(12)-C(4)	113.80(9)
H(2A)-C(2)-H(2B)	107.1(13)	C(16)-C(12)-C(22)	107.86(8)
C(10)-C(3)-C(2)	123.48(10)	C(13)-C(12)-C(22)	106.18(8)
C(10)-C(3)-C(4)	128.15(10)	C(4)-C(12)-C(22)	110.86(9)
C(2)-C(3)-C(4)	108.29(9)	C(14)-C(13)-C(12)	100.65(8)
C(3)-C(4)-C(12)	115.59(9)	C(14)-C(13)-H(13A)	109.4(8)
C(3)-C(4)-C(5)	102.46(9)	C(12)-C(13)-H(13A)	111.7(8)
C(12)-C(4)-C(5)	115.97(9)	C(14)-C(13)-H(13B)	113.1(8)
C(3)-C(4)-H(4)	107.3(8)	C(12)-C(13)-H(13B)	112.3(8)
C(12)-C(4)-H(4)	108.5(8)	H(13A)-C(13)-H(13B)	109.5(11)
C(5)-C(4)-H(4)	106.2(8)	C(21)-C(14)-C(19)	107.97(9)
C(1)-C(5)-C(4)	102.75(9)	C(21)-C(14)-C(13)	107.51(9)
C(1)-C(5)-H(5A)	111.2(8)	C(19)-C(14)-C(13)	115.13(9)
C(4)-C(5)-H(5A)	114.4(8)	C(21)-C(14)-C(15)	109.19(9)
C(1)-C(5)-H(5B)	108.1(8)	C(19)-C(14)-C(15)	112.67(9)
C(4)-C(5)-H(5B)	111.9(8)	C(13)-C(14)-C(15)	104.14(9)
H(5A)-C(5)-H(5B)	108.3(12)	C(16)-C(15)-C(14)	103.94(9)
O(1)-C(6)-O(2)	123.94(11)	C(16)-C(15)-H(15A)	112.2(9)
O(1)-C(6)-C(1)	125.23(10)	C(14)-C(15)-H(15A)	112.1(9)
O(2)-C(6)-C(1)	110.83(9)	C(16)-C(15)-H(15B)	111.0(9)
O(2)-C(7)-H(7A)	105.1(12)	C(14)-C(15)-H(15B)	108.9(9)
O(2)-C(7)-H(7B)	108.3(12)	H(15A)-C(15)-H(15B)	108.6(13)
H(7A)-C(7)-H(7B)	112.3(17)	C(17)-C(16)-C(15)	125.89(10)
O(2)-C(7)-H(7C)	109.4(11)	C(17)-C(16)-C(12)	125.82(10)
H(7A)-C(7)-H(7C)	112.9(17)	C(15)-C(16)-C(12)	108.20(9)
H(7B)-C(7)-H(7C)	108.8(16)	C(16)-C(17)-C(18)	125.70(11)
O(3)-C(8)-O(4)	124.12(11)	C(16)-C(17)-H(17)	118.9(8)
O(3)-C(8)-C(1)	124.22(10)	C(18)-C(17)-H(17)	115.4(8)
O(4)-C(8)-C(1)	111.66(9)	C(17)-C(18)-H(17A)	112.4(10)
O(4)-C(9)-H(9A)	105.2(10)	C(17)-C(18)-H(17B)	109.2(11)
O(4)-C(9)-H(9B)	109.5(10)	H(17A)-C(18)-H(17B)	105.5(15)
H(9A)-C(9)-H(9B)	111.2(14)	C(17)-C(18)-H(17C)	113.3(10)
O(4)-C(9)-H(9C)	109.0(9)	H(17A)-C(18)-H(17C)	107.7(14)

H(17B)-C(18)-H(17C)	108.5(15)	C(24)-C(23)-C(22)	120.31(10)
O(5)-C(19)-O(6)	124.15(10)	C(25)-C(24)-C(23)	120.58(11)
O(5)-C(19)-C(14)	125.12(10)	C(25)-C(24)-H(24)	119.4(9)
O(6)-C(19)-C(14)	110.74(9)	C(23)-C(24)-H(24)	120.0(9)
O(6)-C(20)-H(20A)	109.2(10)	C(26)-C(25)-C(24)	120.35(11)
O(6)-C(20)-H(20B)	104.8(10)	C(26)-C(25)-H(25)	119.9(9)
H(20A)-C(20)-H(20B)	112.6(14)	C(24)-C(25)-H(25)	119.7(9)
O(6)-C(20)-H(20C)	111.4(9)	C(25)-C(26)-C(27)	119.34(11)
H(20A)-C(20)-H(20C)	107.4(14)	C(25)-C(26)-H(26)	120.8(10)
H(20B)-C(20)-H(20C)	111.6(13)	C(27)-C(26)-H(26)	119.8(10)
O(8)-C(21)-O(7)	118.60(10)	C(28)-C(27)-C(26)	120.49(12)
O(8)-C(21)-C(14)	124.16(10)	C(28)-C(27)-H(27)	120.2(10)
O(7)-C(21)-C(14)	117.24(9)	C(26)-C(27)-H(27)	119.3(10)
O(7)-C(22)-C(23)	106.18(8)	C(27)-C(28)-C(23)	120.68(11)
O(7)-C(22)-C(12)	112.71(8)	C(27)-C(28)-H(28)	119.8(9)
C(23)-C(22)-C(12)	115.00(9)	C(23)-C(28)-H(28)	119.6(9)
O(7)-C(22)-H(22)	103.0(8)	C(6)-O(2)-C(7)	115.72(10)
C(23)-C(22)-H(22)	110.2(8)	C(8)-O(4)-C(9)	115.50(9)
C(12)-C(22)-H(22)	109.1(8)	C(19)-O(6)-C(20)	115.44(9)
C(28)-C(23)-C(24)	118.56(10)	C(21)-O(7)-C(22)	125.15(8)
C(28)-C(23)-C(22)	121.12(10)		

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for **37a**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	19(1)	21(1)	20(1)	0(1)	0(1)	3(1)
C(2)	20(1)	24(1)	23(1)	2(1)	3(1)	2(1)
C(3)	18(1)	22(1)	17(1)	-2(1)	-1(1)	0(1)
C(4)	17(1)	18(1)	18(1)	0(1)	-1(1)	1(1)
C(5)	19(1)	19(1)	20(1)	1(1)	-1(1)	1(1)
C(6)	21(1)	20(1)	23(1)	0(1)	-2(1)	4(1)
C(7)	32(1)	78(1)	26(1)	-12(1)	-6(1)	-6(1)
C(8)	17(1)	23(1)	22(1)	1(1)	0(1)	2(1)
C(9)	31(1)	20(1)	29(1)	3(1)	2(1)	5(1)
C(10)	19(1)	23(1)	23(1)	0(1)	-1(1)	-1(1)
C(11)	23(1)	29(1)	28(1)	2(1)	3(1)	-5(1)
C(12)	17(1)	17(1)	19(1)	0(1)	0(1)	0(1)
C(13)	17(1)	18(1)	19(1)	1(1)	0(1)	0(1)
C(14)	19(1)	18(1)	18(1)	1(1)	0(1)	-1(1)
C(15)	24(1)	17(1)	21(1)	1(1)	-3(1)	-1(1)
C(16)	15(1)	18(1)	21(1)	2(1)	1(1)	-1(1)
C(17)	20(1)	20(1)	22(1)	1(1)	-1(1)	0(1)
C(18)	30(1)	20(1)	26(1)	-2(1)	-5(1)	2(1)

C(19)	15(1)	23(1)	20(1)	1(1)	-1(1)	-1(1)
C(20)	26(1)	32(1)	18(1)	-1(1)	0(1)	-2(1)
C(21)	20(1)	16(1)	18(1)	-2(1)	0(1)	1(1)
C(22)	17(1)	18(1)	18(1)	2(1)	-2(1)	0(1)
C(23)	19(1)	18(1)	21(1)	0(1)	1(1)	-4(1)
C(24)	23(1)	22(1)	23(1)	1(1)	0(1)	1(1)
C(25)	33(1)	30(1)	21(1)	1(1)	-2(1)	2(1)
C(26)	35(1)	37(1)	22(1)	-6(1)	4(1)	6(1)
C(27)	30(1)	36(1)	29(1)	-4(1)	1(1)	11(1)
C(28)	24(1)	27(1)	23(1)	1(1)	-1(1)	4(1)
O(1)	25(1)	39(1)	21(1)	0(1)	2(1)	6(1)
O(2)	24(1)	43(1)	23(1)	-5(1)	-3(1)	-2(1)
O(3)	38(1)	26(1)	23(1)	-2(1)	1(1)	9(1)
O(4)	27(1)	21(1)	22(1)	2(1)	1(1)	4(1)
O(5)	29(1)	24(1)	22(1)	5(1)	0(1)	0(1)
O(6)	27(1)	23(1)	18(1)	0(1)	0(1)	-1(1)
O(7)	17(1)	24(1)	18(1)	3(1)	-2(1)	-2(1)
O(8)	19(1)	24(1)	21(1)	1(1)	-3(1)	1(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^{3}) for **37a**.

	x	y	z	U(eq)
H(2A)	3505(15)	9524(17)	8950(6)	28(4)
H(2B)	4235(15)	10270(17)	9420(6)	29(4)
H(4)	6638(12)	8554(14)	8631(5)	14(3)
H(5A)	7141(14)	11038(15)	8722(5)	21(3)
H(5B)	6628(13)	11035(15)	9296(5)	21(3)
H(7A)	2560(20)	9780(20)	7487(8)	57(5)
H(7B)	3808(19)	10780(20)	7323(8)	53(5)
H(7C)	3978(19)	9020(20)	7412(8)	52(5)
H(9A)	4002(15)	14989(17)	8101(6)	31(4)
H(9B)	4816(16)	15226(18)	8622(6)	33(4)
H(9C)	3345(16)	14694(17)	8631(6)	30(4)
H(10)	5551(14)	6452(17)	9447(5)	25(3)
H(11A)	3681(16)	6792(18)	9972(7)	34(4)
H(11B)	3010(17)	7770(20)	9545(6)	41(4)
H(11C)	3224(16)	6060(19)	9456(6)	35(4)
H(13A)	6841(14)	8179(15)	9995(5)	21(3)
H(13B)	7856(13)	9488(16)	9977(5)	17(3)
H(15A)	9274(15)	5466(17)	9687(6)	29(4)
H(15B)	7843(15)	5369(17)	9903(6)	28(4)
H(17)	7354(14)	6371(16)	8499(6)	24(3)
H(17A)	7204(17)	3736(19)	8580(6)	39(4)

H(17B)	8669(19)	4120(20)	8506(7)	51(5)
H(17C)	8172(16)	3765(19)	9057(7)	37(4)
H(20A)	9521(17)	7649(19)	11548(6)	36(4)
H(20B)	8660(16)	9100(20)	11588(6)	35(4)
H(20C)	8027(15)	7509(17)	11573(6)	28(4)
H(22)	8927(12)	10073(15)	9137(5)	15(3)
H(24)	8338(15)	9818(17)	8179(6)	28(4)
H(25)	9098(15)	9045(17)	7388(6)	33(4)
H(26)	10797(17)	7323(19)	7361(7)	39(4)
H(27)	11677(17)	6340(20)	8123(6)	40(4)
H(28)	10898(14)	7072(16)	8919(6)	25(3)

Dimethyl (3*Z*)-3-[4,4-bis(methoxycarbonyl)-2-methylenecyclopentylidene]-4-[(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl]cyclohexane-1,1-dicarboxylate (48)

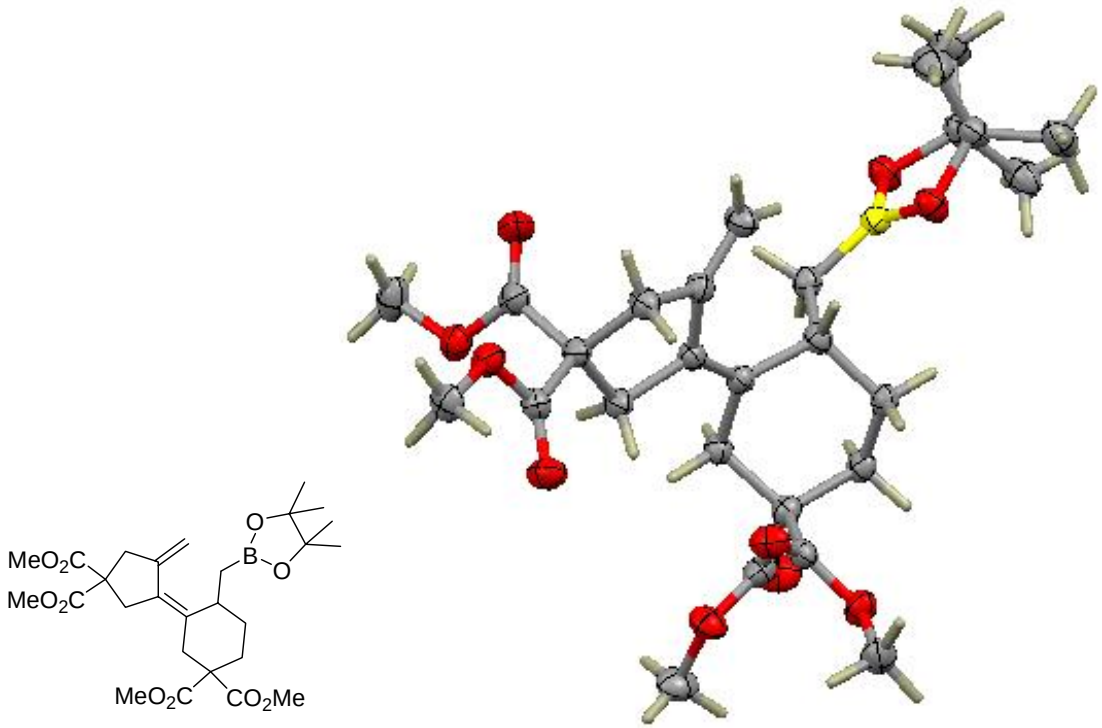


Table 1. Crystal data and structure refinement for **48**.

Empirical formula	C27 H39 B O10	
Formula weight	534.39	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 10.4461(2) Å	α= 106.6130(10)°.
	b = 11.4808(2) Å	β= 103.6150(10)°.
	c = 13.6972(3) Å	γ = 108.9590(10)°.
Volume	1387.63(5) $Å^3$	
Z	2	
Density (calculated)	1.279 Mg/m^3	
Absorption coefficient	0.798 mm^{-1}	
F(000)	572	
Crystal size	0.25 x 0.22 x 0.18 mm^3	
Theta range for data collection	3.61 to 68.32°.	
Index ranges	-12<=h<=12, -13<=k<=13, -16<=l<=16	
Reflections collected	15147	
Independent reflections	4854 [R(int) = 0.0238]	
Completeness to theta = 68.32°	95.2 %	
Absorption correction	Semi-empirical from equivalents	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4854 / 0 / 499	
Goodness-of-fit on F^2	1.035	
Final R indices [I>2sigma(I)]	R1 = 0.0380, wR2 = 0.1010	
R indices (all data)	R1 = 0.0404, wR2 = 0.1037	
Largest diff. peak and hole	0.298 and -0.179 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **48**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
B(1)	4394(2)	3000(2)	3508(1)	25(1)
C(1)	2910(2)	1553(1)	4032(1)	31(1)
C(2)	2146(1)	1274(1)	2816(1)	31(1)
C(3)	3545(2)	566(2)	4166(2)	42(1)
C(4)	2007(2)	1681(2)	4743(2)	47(1)
C(5)	1473(2)	-191(2)	2046(1)	41(1)

C(6)	1061(2)	1872(2)	2638(2)	48(1)
C(7)	5719(1)	4194(1)	3561(1)	26(1)
C(8)	5939(1)	4014(1)	2457(1)	25(1)
C(9)	6535(1)	2952(1)	2133(1)	26(1)
C(10)	8135(1)	3429(1)	2801(1)	27(1)
C(11)	9069(1)	4699(1)	2699(1)	25(1)
C(12)	8523(1)	5790(1)	3066(1)	25(1)
C(13)	6915(1)	5332(1)	2476(1)	24(1)
C(14)	9024(1)	4408(1)	1528(1)	25(1)
C(15)	9628(2)	3178(2)	150(1)	37(1)
C(16)	10651(1)	5246(1)	3442(1)	28(1)
C(17)	13048(2)	6722(2)	3803(2)	42(1)
C(18)	6441(1)	6098(1)	2046(1)	24(1)
C(19)	7464(1)	7354(1)	1991(1)	26(1)
C(20)	6491(1)	7981(1)	1528(1)	26(1)
C(21)	5010(1)	6774(1)	849(1)	29(1)
C(22)	4929(1)	5877(1)	1480(1)	26(1)
C(23)	6383(2)	9013(1)	2458(1)	29(1)
C(24)	7740(2)	11095(2)	3957(1)	41(1)
C(25)	7066(1)	8658(1)	816(1)	26(1)
C(26)	6814(2)	10085(2)	-79(1)	34(1)
C(27)	3676(2)	5132(1)	1515(1)	33(1)
O(1)	4135(1)	2853(1)	4412(1)	32(1)
O(2)	3356(1)	2009(1)	2552(1)	32(1)
O(3)	8595(1)	4915(1)	950(1)	33(1)
O(4)	9540(1)	3489(1)	1226(1)	32(1)
O(5)	11070(1)	4966(1)	4200(1)	41(1)
O(6)	11514(1)	6123(1)	3155(1)	36(1)
O(7)	5315(1)	8927(1)	2665(1)	46(1)
O(8)	7690(1)	10049(1)	3047(1)	33(1)
O(9)	7974(1)	8526(1)	462(1)	37(1)
O(10)	6366(1)	9405(1)	607(1)	31(1)

Table 3. Bond lengths [Å] and angles [°] for **48**.

B(1)-O(2)	1.3652(19)	C(3)-H(3A)	0.98(2)
B(1)-O(1)	1.3710(18)	C(3)-H(3B)	1.01(2)
B(1)-C(7)	1.5695(19)	C(3)-H(3C)	0.99(2)
C(1)-O(1)	1.4616(16)	C(4)-H(4A)	1.02(2)
C(1)-C(4)	1.517(2)	C(4)-H(4B)	0.99(2)
C(1)-C(3)	1.518(2)	C(4)-H(4C)	0.993(19)
C(1)-C(2)	1.554(2)	C(5)-H(5A)	1.03(2)
C(2)-O(2)	1.4616(16)	C(5)-H(5B)	1.02(2)
C(2)-C(6)	1.512(2)	C(5)-H(5C)	1.007(19)
C(2)-C(5)	1.517(2)	C(6)-H(6A)	0.99(2)

C(6)-H(6B)	0.97(2)	C(23)-O(8)	1.3442(17)
C(6)-H(6C)	0.99(2)	C(24)-O(8)	1.4386(18)
C(7)-C(8)	1.5480(18)	C(24)-H(24A)	0.96(2)
C(7)-H(7A)	0.993(17)	C(24)-H(24B)	0.97(2)
C(7)-H(7B)	0.960(16)	C(24)-H(24C)	0.993(19)
C(8)-C(13)	1.5137(17)	C(25)-O(9)	1.1944(16)
C(8)-C(9)	1.5442(17)	C(25)-O(10)	1.3424(16)
C(8)-H(8)	0.970(14)	C(26)-O(10)	1.4495(16)
C(9)-C(10)	1.5256(18)	C(26)-H(26A)	0.982(19)
C(9)-H(9A)	1.001(16)	C(26)-H(26B)	0.96(2)
C(9)-H(9B)	0.979(16)	C(26)-H(26C)	0.99(2)
C(10)-C(11)	1.5337(17)	C(27)-H(27A)	0.977(18)
C(10)-H(10A)	0.979(17)	C(27)-H(27B)	0.979(16)
C(10)-H(10B)	0.998(16)	O(2)-B(1)-O(1)	112.72(12)
C(11)-C(16)	1.5260(18)	O(2)-B(1)-C(7)	123.32(12)
C(11)-C(14)	1.5283(18)	O(1)-B(1)-C(7)	123.94(12)
C(11)-C(12)	1.5451(17)	O(1)-C(1)-C(4)	108.36(12)
C(12)-C(13)	1.5148(17)	O(1)-C(1)-C(3)	106.88(11)
C(12)-H(12A)	0.964(16)	C(4)-C(1)-C(3)	110.22(13)
C(12)-H(12B)	0.973(16)	O(1)-C(1)-C(2)	102.41(10)
C(13)-C(18)	1.3442(18)	C(4)-C(1)-C(2)	115.20(13)
C(14)-O(3)	1.1977(16)	C(3)-C(1)-C(2)	113.06(13)
C(14)-O(4)	1.3417(16)	O(2)-C(2)-C(6)	106.55(12)
C(15)-O(4)	1.4465(17)	O(2)-C(2)-C(5)	108.67(11)
C(15)-H(15A)	0.973(18)	C(6)-C(2)-C(5)	110.30(13)
C(15)-H(15B)	1.003(19)	O(2)-C(2)-C(1)	101.92(10)
C(15)-H(15C)	0.951(19)	C(6)-C(2)-C(1)	114.21(14)
C(16)-O(5)	1.2003(17)	C(5)-C(2)-C(1)	114.42(12)
C(16)-O(6)	1.3356(17)	C(1)-C(3)-H(3A)	110.7(11)
C(17)-O(6)	1.4477(17)	C(1)-C(3)-H(3B)	109.6(12)
C(17)-H(17A)	1.00(2)	H(3A)-C(3)-H(3B)	109.4(17)
C(17)-H(17B)	0.94(2)	C(1)-C(3)-H(3C)	110.3(11)
C(17)-H(17C)	0.971(19)	H(3A)-C(3)-H(3C)	108.3(16)
C(18)-C(22)	1.4873(17)	H(3B)-C(3)-H(3C)	108.6(16)
C(18)-C(19)	1.5259(17)	C(1)-C(4)-H(4A)	106.4(13)
C(19)-C(20)	1.5443(17)	C(1)-C(4)-H(4B)	109.9(11)
C(19)-H(19A)	1.000(17)	H(4A)-C(4)-H(4B)	112.8(17)
C(19)-H(19B)	0.963(17)	C(1)-C(4)-H(4C)	107.7(10)
C(20)-C(25)	1.5235(17)	H(4A)-C(4)-H(4C)	113.7(17)
C(20)-C(23)	1.5266(19)	H(4B)-C(4)-H(4C)	106.2(15)
C(20)-C(21)	1.5400(18)	C(2)-C(5)-H(5A)	110.4(11)
C(21)-C(22)	1.5171(17)	C(2)-C(5)-H(5B)	109.4(12)
C(21)-H(21A)	1.006(18)	H(5A)-C(5)-H(5B)	109.0(16)
C(21)-H(21B)	0.967(18)	C(2)-C(5)-H(5C)	108.6(10)
C(22)-C(27)	1.3309(19)	H(5A)-C(5)-H(5C)	106.4(15)
C(23)-O(7)	1.1953(17)	H(5B)-C(5)-H(5C)	113.0(16)

C(2)-C(6)-H(6A)	111.0(11)	O(3)-C(14)-C(11)	125.80(12)
C(2)-C(6)-H(6B)	104.3(12)	O(4)-C(14)-C(11)	110.21(10)
H(6A)-C(6)-H(6B)	113.0(16)	O(4)-C(15)-H(15A)	109.9(10)
C(2)-C(6)-H(6C)	109.5(11)	O(4)-C(15)-H(15B)	104.5(11)
H(6A)-C(6)-H(6C)	106.6(16)	H(15A)-C(15)-H(15B)	113.9(15)
H(6B)-C(6)-H(6C)	112.4(16)	O(4)-C(15)-H(15C)	110.1(11)
C(8)-C(7)-B(1)	114.38(11)	H(15A)-C(15)-H(15C)	108.3(15)
C(8)-C(7)-H(7A)	110.2(9)	H(15B)-C(15)-H(15C)	110.2(15)
B(1)-C(7)-H(7A)	105.7(9)	O(5)-C(16)-O(6)	124.23(12)
C(8)-C(7)-H(7B)	110.8(9)	O(5)-C(16)-C(11)	125.31(12)
B(1)-C(7)-H(7B)	110.9(9)	O(6)-C(16)-C(11)	110.42(10)
H(7A)-C(7)-H(7B)	104.3(13)	O(6)-C(17)-H(17A)	111.4(11)
C(13)-C(8)-C(9)	110.53(10)	O(6)-C(17)-H(17B)	104.6(12)
C(13)-C(8)-C(7)	111.39(10)	H(17A)-C(17)-H(17B)	114.4(17)
C(9)-C(8)-C(7)	111.91(10)	O(6)-C(17)-H(17C)	108.7(11)
C(13)-C(8)-H(8)	108.4(8)	H(17A)-C(17)-H(17C)	107.1(16)
C(9)-C(8)-H(8)	106.3(8)	H(17B)-C(17)-H(17C)	110.6(16)
C(7)-C(8)-H(8)	108.1(8)	C(13)-C(18)-C(22)	129.42(11)
C(10)-C(9)-C(8)	113.67(11)	C(13)-C(18)-C(19)	122.84(11)
C(10)-C(9)-H(9A)	108.1(8)	C(22)-C(18)-C(19)	107.57(10)
C(8)-C(9)-H(9A)	109.6(8)	C(18)-C(19)-C(20)	105.87(10)
C(10)-C(9)-H(9B)	109.3(9)	C(18)-C(19)-H(19A)	113.9(9)
C(8)-C(9)-H(9B)	108.6(9)	C(20)-C(19)-H(19A)	110.9(9)
H(9A)-C(9)-H(9B)	107.3(12)	C(18)-C(19)-H(19B)	110.8(9)
C(9)-C(10)-C(11)	110.59(10)	C(20)-C(19)-H(19B)	109.0(9)
C(9)-C(10)-H(10A)	110.6(9)	H(19A)-C(19)-H(19B)	106.4(13)
C(11)-C(10)-H(10A)	106.8(9)	C(25)-C(20)-C(23)	108.82(10)
C(9)-C(10)-H(10B)	109.8(9)	C(25)-C(20)-C(21)	111.02(11)
C(11)-C(10)-H(10B)	109.4(9)	C(23)-C(20)-C(21)	111.16(11)
H(10A)-C(10)-H(10B)	109.7(13)	C(25)-C(20)-C(19)	111.97(10)
C(16)-C(11)-C(14)	107.72(10)	C(23)-C(20)-C(19)	110.30(11)
C(16)-C(11)-C(10)	110.68(10)	C(21)-C(20)-C(19)	103.53(10)
C(14)-C(11)-C(10)	111.00(11)	C(22)-C(21)-C(20)	103.93(10)
C(16)-C(11)-C(12)	107.66(10)	C(22)-C(21)-H(21A)	111.0(10)
C(14)-C(11)-C(12)	110.54(10)	C(20)-C(21)-H(21A)	107.4(9)
C(10)-C(11)-C(12)	109.18(10)	C(22)-C(21)-H(21B)	112.3(10)
C(13)-C(12)-C(11)	113.52(11)	C(20)-C(21)-H(21B)	112.6(10)
C(13)-C(12)-H(12A)	112.8(9)	H(21A)-C(21)-H(21B)	109.5(14)
C(11)-C(12)-H(12A)	107.8(9)	C(27)-C(22)-C(18)	130.79(12)
C(13)-C(12)-H(12B)	108.2(9)	C(27)-C(22)-C(21)	121.79(12)
C(11)-C(12)-H(12B)	106.2(9)	C(18)-C(22)-C(21)	107.30(10)
H(12A)-C(12)-H(12B)	108.0(12)	O(7)-C(23)-O(8)	123.60(13)
C(18)-C(13)-C(8)	124.59(11)	O(7)-C(23)-C(20)	126.21(13)
C(18)-C(13)-C(12)	120.29(11)	O(8)-C(23)-C(20)	110.17(11)
C(8)-C(13)-C(12)	115.08(10)	O(8)-C(24)-H(24A)	111.7(13)
O(3)-C(14)-O(4)	123.99(12)	O(8)-C(24)-H(24B)	108.1(12)

H(24A)-C(24)-H(24B)	111.3(17)	H(26A)-C(26)-H(26C)	110.4(15)
O(8)-C(24)-H(24C)	108.8(11)	H(26B)-C(26)-H(26C)	111.5(15)
H(24A)-C(24)-H(24C)	105.1(17)	C(22)-C(27)-H(27A)	123.3(10)
H(24B)-C(24)-H(24C)	111.9(15)	C(22)-C(27)-H(27B)	118.9(9)
O(9)-C(25)-O(10)	124.03(12)	H(27A)-C(27)-H(27B)	117.7(14)
O(9)-C(25)-C(20)	125.93(11)	B(1)-O(1)-C(1)	107.28(10)
O(10)-C(25)-C(20)	110.00(10)	B(1)-O(2)-C(2)	107.41(10)
O(10)-C(26)-H(26A)	110.0(10)	C(14)-O(4)-C(15)	115.56(11)
O(10)-C(26)-H(26B)	106.0(11)	C(16)-O(6)-C(17)	115.87(12)
H(26A)-C(26)-H(26B)	110.0(15)	C(23)-O(8)-C(24)	115.82(12)
O(10)-C(26)-H(26C)	108.9(11)	C(25)-O(10)-C(26)	114.80(10)

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for **48**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
B(1)	26(1)	26(1)	26(1)	11(1)	10(1)	13(1)
C(1)	30(1)	30(1)	32(1)	12(1)	14(1)	7(1)
C(2)	27(1)	31(1)	33(1)	13(1)	13(1)	8(1)
C(3)	38(1)	40(1)	50(1)	28(1)	15(1)	12(1)
C(4)	47(1)	43(1)	41(1)	10(1)	27(1)	6(1)
C(5)	39(1)	34(1)	37(1)	8(1)	15(1)	4(1)
C(6)	32(1)	47(1)	65(1)	26(1)	12(1)	17(1)
C(7)	28(1)	26(1)	26(1)	10(1)	10(1)	11(1)
C(8)	24(1)	25(1)	26(1)	12(1)	8(1)	10(1)
C(9)	31(1)	22(1)	26(1)	11(1)	12(1)	10(1)
C(10)	33(1)	28(1)	28(1)	15(1)	14(1)	16(1)
C(11)	25(1)	26(1)	25(1)	11(1)	8(1)	12(1)
C(12)	26(1)	23(1)	26(1)	10(1)	8(1)	10(1)
C(13)	24(1)	24(1)	23(1)	9(1)	9(1)	10(1)
C(14)	21(1)	24(1)	27(1)	10(1)	8(1)	7(1)
C(15)	44(1)	35(1)	32(1)	12(1)	21(1)	14(1)
C(16)	30(1)	31(1)	25(1)	9(1)	10(1)	18(1)
C(17)	25(1)	49(1)	39(1)	8(1)	6(1)	12(1)
C(18)	24(1)	22(1)	24(1)	9(1)	10(1)	9(1)
C(19)	24(1)	25(1)	32(1)	14(1)	10(1)	11(1)
C(20)	26(1)	25(1)	30(1)	14(1)	12(1)	12(1)
C(21)	26(1)	30(1)	33(1)	16(1)	10(1)	12(1)
C(22)	26(1)	24(1)	27(1)	10(1)	9(1)	11(1)
C(23)	35(1)	28(1)	33(1)	19(1)	18(1)	16(1)
C(24)	64(1)	30(1)	33(1)	14(1)	24(1)	20(1)
C(25)	27(1)	23(1)	26(1)	10(1)	8(1)	9(1)
C(26)	45(1)	33(1)	35(1)	21(1)	19(1)	17(1)
C(27)	27(1)	33(1)	41(1)	19(1)	12(1)	13(1)

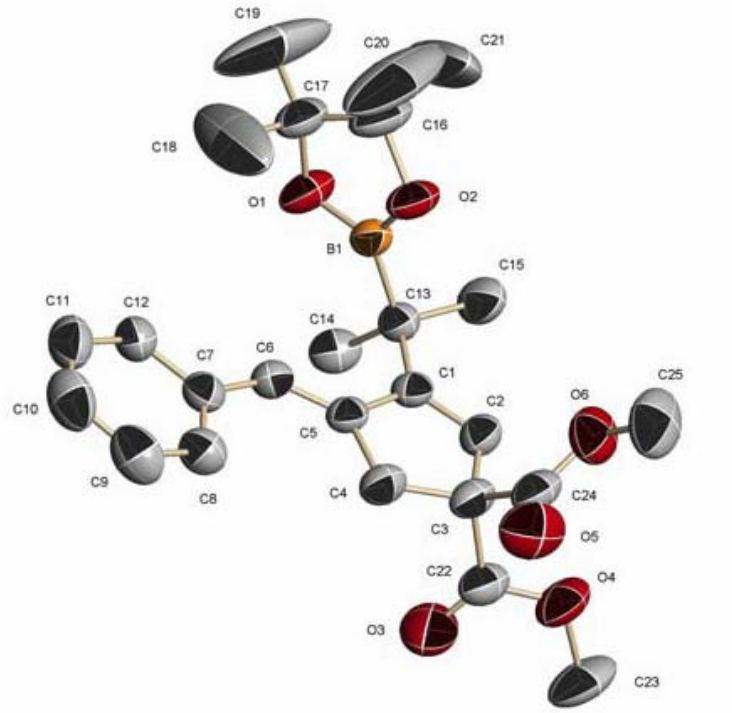
O(1)	31(1)	30(1)	26(1)	9(1)	11(1)	6(1)
O(2)	31(1)	32(1)	28(1)	12(1)	12(1)	7(1)
O(3)	35(1)	46(1)	31(1)	23(1)	16(1)	23(1)
O(4)	43(1)	29(1)	30(1)	13(1)	19(1)	18(1)
O(5)	37(1)	59(1)	32(1)	22(1)	9(1)	24(1)
O(6)	25(1)	39(1)	37(1)	15(1)	6(1)	10(1)
O(7)	46(1)	38(1)	61(1)	17(1)	35(1)	19(1)
O(8)	39(1)	28(1)	30(1)	9(1)	14(1)	13(1)
O(9)	37(1)	46(1)	45(1)	27(1)	24(1)	23(1)
O(10)	40(1)	33(1)	35(1)	22(1)	20(1)	21(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3) for **48**.

	x	y	z	U(eq)
H(3A)	2770(20)	-330(20)	3927(16)	51(5)
H(3B)	4160(20)	880(20)	4959(18)	55(5)
H(3C)	4160(20)	505(18)	3720(16)	46(5)
H(4A)	2670(20)	1940(20)	5520(20)	66(6)
H(4B)	1130(20)	830(20)	4468(16)	47(5)
H(4C)	1653(19)	2365(19)	4659(14)	39(4)
H(5A)	700(20)	-758(19)	2275(16)	50(5)
H(5B)	990(20)	-290(20)	1272(18)	56(5)
H(5C)	2250(20)	-532(18)	2114(15)	42(5)
H(6A)	170(20)	1376(19)	2753(15)	47(5)
H(6B)	870(20)	1820(20)	1892(18)	53(5)
H(6C)	1490(20)	2800(20)	3180(16)	46(5)
H(7A)	5532(17)	5001(17)	3824(13)	31(4)
H(7B)	6595(17)	4378(15)	4121(13)	26(4)
H(8)	4997(16)	3679(14)	1892(12)	19(3)
H(9A)	6416(16)	2685(15)	1343(13)	24(3)
H(9B)	5956(17)	2151(16)	2218(13)	29(4)
H(10A)	8289(17)	3663(16)	3578(14)	31(4)
H(10B)	8460(16)	2711(16)	2538(13)	28(4)
H(12A)	9118(16)	6574(15)	2989(12)	25(4)
H(12B)	8702(16)	6012(15)	3840(14)	25(4)
H(15A)	8660(20)	2775(17)	-403(15)	37(4)
H(15B)	10140(20)	2570(19)	102(15)	45(5)
H(15C)	10190(20)	3975(19)	89(15)	43(5)
H(17A)	13250(20)	7260(20)	4581(18)	49(5)
H(17B)	13500(20)	7220(20)	3440(17)	52(5)
H(17C)	13360(19)	6011(19)	3801(15)	42(5)
H(19A)	8240(17)	8015(16)	2710(13)	26(4)
H(19B)	7956(17)	7128(15)	1502(13)	29(4)

H(21A)	5039(18)	6326(17)	112(15)	35(4)
H(21B)	4209(19)	7031(16)	757(14)	36(4)
H(24A)	7480(20)	10770(20)	4486(18)	60(6)
H(24B)	8710(20)	11810(20)	4278(16)	47(5)
H(24C)	7000(20)	11405(18)	3690(15)	42(5)
H(26A)	6724(18)	9434(18)	-766(15)	37(4)
H(26B)	6170(20)	10496(19)	-226(15)	44(5)
H(26C)	7840(20)	10764(19)	322(15)	43(5)
H(27A)	3598(19)	4557(18)	1924(15)	41(4)
H(27B)	2784(18)	5169(16)	1124(13)	31(4)

(*E*)-Dimethyl 4-benzylidene-3-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propan-2-yl)cyclopent-2-ene-1,1-dicarboxylate (61f)



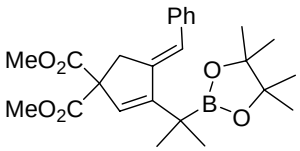


Table 1. Crystal data and structure refinement for **61f**.

Empirical formula	C25 H33 B O6	
Formula weight	440.32	
Temperature	296(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	Pbca	
Unit cell dimensions	a = 12.528(8) Å	α= 90°.

	b = 15.977(12) Å	β= 90°.
	c = 24.44(2) Å	γ = 90°.
Volume	4892(6) $Å^3$	
Z	8	
Density (calculated)	1.196 Mg/m^3	
Absorption coefficient	0.083 mm^{-1}	
F(000)	1888	
Crystal size	0.30 x 0.25 x 0.25 mm^3	
Theta range for data collection	1.67 to 25.68°.	
Index ranges	-15<=h<=15, -18<=k<=19, -29<=l<=29	
Reflections collected	32699	
Independent reflections	4649 [R(int) = 0.0908]	
Completeness to theta = 25.68°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9795 and 0.9754	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4649 / 0 / 298	
Goodness-of-fit on F^2	1.018	
Final R indices [I>2sigma(I)]	R1 = 0.0713, wR2 = 0.1963	
R indices (all data)	R1 = 0.1397, wR2 = 0.2680	
Extinction coefficient	0.0110(15)	
Largest diff. peak and hole	0.715 and -0.258 e.$Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **61f**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
B(1)	5663(3)	1780(3)	3152(2)	49(1)
C(1)	5130(3)	3282(2)	3388(1)	47(1)
C(2)	4247(3)	3737(2)	3453(2)	54(1)
C(3)	4276(3)	4292(2)	3940(2)	55(1)
C(4)	5372(3)	4096(2)	4200(2)	57(1)
C(5)	5886(3)	3448(2)	3834(1)	47(1)
C(6)	6829(3)	3071(2)	3900(2)	50(1)
C(7)	7628(3)	3116(2)	4331(2)	52(1)
C(8)	7570(3)	3636(3)	4781(2)	63(1)
C(9)	8336(4)	3591(3)	5184(2)	80(1)
C(10)	9175(4)	3035(4)	5150(2)	83(1)
C(11)	9258(3)	2533(3)	4699(2)	76(1)
C(12)	8499(3)	2575(3)	4296(2)	61(1)

C(13)	5372(3)	2676(2)	2934(2)	49(1)
C(14)	6273(3)	3029(3)	2571(2)	63(1)
C(15)	4373(3)	2534(3)	2575(2)	70(1)
C(16)	5437(4)	487(3)	3508(3)	97(2)
C(17)	6511(4)	537(2)	3261(2)	74(1)
C(18)	7285(8)	662(5)	3755(5)	229(7)
C(19)	6924(9)	-123(4)	2928(4)	220(6)
C(20)	5164(8)	44(5)	3959(5)	243(8)
C(21)	4703(8)	44(5)	3044(7)	285(9)
C(22)	4190(4)	5199(3)	3755(2)	66(1)
C(23)	3010(5)	6249(3)	3452(2)	103(2)
C(24)	3368(3)	4151(3)	4345(2)	65(1)
C(25)	1779(4)	3444(4)	4535(3)	109(2)
O(1)	6513(2)	1337(2)	2981(1)	72(1)
O(2)	5044(2)	1338(2)	3501(1)	74(1)
O(3)	4921(3)	5662(2)	3696(2)	129(2)
O(4)	3198(2)	5407(2)	3647(1)	83(1)
O(5)	3347(3)	4472(2)	4784(2)	100(1)
O(6)	2654(2)	3627(2)	4167(1)	82(1)

Table 3. Bond lengths [Å] and angles [°]for **61f**.

B(1)-O(1)	1.345(5)	C(9)-H(9)	0.9300
B(1)-O(2)	1.352(5)	C(10)-C(11)	1.366(7)
B(1)-C(13)	1.571(5)	C(10)-H(10)	0.9300
C(1)-C(2)	1.333(5)	C(11)-C(12)	1.371(6)
C(1)-C(5)	1.469(5)	C(11)-H(11)	0.9300
C(1)-C(13)	1.502(5)	C(12)-H(12)	0.9300
C(2)-C(3)	1.483(6)	C(13)-C(14)	1.542(5)
C(2)-H(2)	0.9300	C(13)-C(15)	1.546(5)
C(3)-C(22)	1.522(6)	C(14)-H(14A)	0.9600
C(3)-C(24)	1.526(6)	C(14)-H(14B)	0.9600
C(3)-C(4)	1.546(5)	C(14)-H(14C)	0.9600
C(4)-C(5)	1.512(5)	C(15)-H(15A)	0.9600
C(4)-H(4A)	0.9700	C(15)-H(15B)	0.9600
C(4)-H(4B)	0.9700	C(15)-H(15C)	0.9600
C(5)-C(6)	1.337(5)	C(16)-C(20)	1.355(9)
C(6)-C(7)	1.454(5)	C(16)-O(2)	1.446(5)
C(6)-H(6)	0.9300	C(16)-C(17)	1.477(7)
C(7)-C(8)	1.381(5)	C(16)-C(21)	1.622(11)
C(7)-C(12)	1.395(5)	C(17)-C(19)	1.429(8)
C(8)-C(9)	1.378(6)	C(17)-O(1)	1.451(5)
C(8)-H(8)	0.9300	C(17)-C(18)	1.562(9)
C(9)-C(10)	1.379(7)	C(18)-H(18A)	0.9600

C(18)-H(18B)	0.9600	C(1)-C(5)-C(4)	106.8(3)
C(18)-H(18C)	0.9600	C(5)-C(6)-C(7)	132.4(3)
C(19)-H(19A)	0.9600	C(5)-C(6)-H(6)	113.8
C(19)-H(19B)	0.9600	C(7)-C(6)-H(6)	113.8
C(19)-H(19C)	0.9600	C(8)-C(7)-C(12)	117.6(4)
C(20)-H(20A)	0.9600	C(8)-C(7)-C(6)	124.7(3)
C(20)-H(20B)	0.9600	C(12)-C(7)-C(6)	117.7(3)
C(20)-H(20C)	0.9600	C(9)-C(8)-C(7)	120.1(4)
C(21)-H(21A)	0.9600	C(9)-C(8)-H(8)	119.9
C(21)-H(21B)	0.9600	C(7)-C(8)-H(8)	119.9
C(21)-H(21C)	0.9600	C(8)-C(9)-C(10)	121.4(4)
C(22)-O(3)	1.186(5)	C(8)-C(9)-H(9)	119.3
C(22)-O(4)	1.313(5)	C(10)-C(9)-H(9)	119.3
C(23)-O(4)	1.446(5)	C(11)-C(10)-C(9)	119.1(4)
C(23)-H(23A)	0.9600	C(11)-C(10)-H(10)	120.5
C(23)-H(23B)	0.9600	C(9)-C(10)-H(10)	120.5
C(23)-H(23C)	0.9600	C(10)-C(11)-C(12)	119.9(4)
C(24)-O(5)	1.189(5)	C(10)-C(11)-H(11)	120.1
C(24)-O(6)	1.301(5)	C(12)-C(11)-H(11)	120.1
C(25)-O(6)	1.449(5)	C(11)-C(12)-C(7)	121.9(4)
C(25)-H(25A)	0.9600	C(11)-C(12)-H(12)	119.0
C(25)-H(25B)	0.9600	C(7)-C(12)-H(12)	119.0
C(25)-H(25C)	0.9600	C(1)-C(13)-C(14)	109.7(3)
O(1)-B(1)-O(2)	112.1(3)	C(1)-C(13)-C(15)	110.5(3)
O(1)-B(1)-C(13)	123.9(4)	C(14)-C(13)-C(15)	108.7(3)
O(2)-B(1)-C(13)	123.9(3)	C(1)-C(13)-B(1)	112.6(3)
C(2)-C(1)-C(5)	110.2(3)	C(14)-C(13)-B(1)	111.0(3)
C(2)-C(1)-C(13)	127.4(3)	C(15)-C(13)-B(1)	104.3(3)
C(5)-C(1)-C(13)	122.3(3)	C(13)-C(14)-H(14A)	109.5
C(1)-C(2)-C(3)	113.7(3)	C(13)-C(14)-H(14B)	109.5
C(1)-C(2)-H(2)	123.1	H(14A)-C(14)-H(14B)	109.5
C(3)-C(2)-H(2)	123.1	C(13)-C(14)-H(14C)	109.5
C(2)-C(3)-C(22)	109.3(3)	H(14A)-C(14)-H(14C)	109.5
C(2)-C(3)-C(24)	114.5(3)	H(14B)-C(14)-H(14C)	109.5
C(22)-C(3)-C(24)	106.2(3)	C(13)-C(15)-H(15A)	109.5
C(2)-C(3)-C(4)	103.3(3)	C(13)-C(15)-H(15B)	109.5
C(22)-C(3)-C(4)	112.2(3)	H(15A)-C(15)-H(15B)	109.5
C(24)-C(3)-C(4)	111.4(3)	C(13)-C(15)-H(15C)	109.5
C(5)-C(4)-C(3)	105.8(3)	H(15A)-C(15)-H(15C)	109.5
C(5)-C(4)-H(4A)	110.6	H(15B)-C(15)-H(15C)	109.5
C(3)-C(4)-H(4A)	110.6	C(20)-C(16)-O(2)	114.5(5)
C(5)-C(4)-H(4B)	110.6	C(20)-C(16)-C(17)	126.1(6)
C(3)-C(4)-H(4B)	110.6	O(2)-C(16)-C(17)	104.8(4)
H(4A)-C(4)-H(4B)	108.7	C(20)-C(16)-C(21)	101.5(8)
C(6)-C(5)-C(1)	125.3(3)	O(2)-C(16)-C(21)	102.1(5)
C(6)-C(5)-C(4)	127.8(3)	C(17)-C(16)-C(21)	104.8(7)

C(19)-C(17)-O(1)	112.3(5)	H(21A)-C(21)-H(21B)	109.5
C(19)-C(17)-C(16)	121.5(6)	C(16)-C(21)-H(21C)	109.5
O(1)-C(17)-C(16)	104.0(3)	H(21A)-C(21)-H(21C)	109.5
C(19)-C(17)-C(18)	108.1(7)	H(21B)-C(21)-H(21C)	109.5
O(1)-C(17)-C(18)	104.6(4)	O(3)-C(22)-O(4)	123.2(4)
C(16)-C(17)-C(18)	104.9(6)	O(3)-C(22)-C(3)	125.1(4)
C(17)-C(18)-H(18A)	109.5	O(4)-C(22)-C(3)	111.6(4)
C(17)-C(18)-H(18B)	109.5	O(4)-C(23)-H(23A)	109.5
H(18A)-C(18)-H(18B)	109.5	O(4)-C(23)-H(23B)	109.5
C(17)-C(18)-H(18C)	109.5	H(23A)-C(23)-H(23B)	109.5
H(18A)-C(18)-H(18C)	109.5	O(4)-C(23)-H(23C)	109.5
H(18B)-C(18)-H(18C)	109.5	H(23A)-C(23)-H(23C)	109.5
C(17)-C(19)-H(19A)	109.5	H(23B)-C(23)-H(23C)	109.5
C(17)-C(19)-H(19B)	109.5	O(5)-C(24)-O(6)	124.4(4)
H(19A)-C(19)-H(19B)	109.5	O(5)-C(24)-C(3)	122.6(4)
C(17)-C(19)-H(19C)	109.5	O(6)-C(24)-C(3)	113.0(4)
H(19A)-C(19)-H(19C)	109.5	O(6)-C(25)-H(25A)	109.5
H(19B)-C(19)-H(19C)	109.5	O(6)-C(25)-H(25B)	109.5
C(16)-C(20)-H(20A)	109.5	H(25A)-C(25)-H(25B)	109.5
C(16)-C(20)-H(20B)	109.5	O(6)-C(25)-H(25C)	109.5
H(20A)-C(20)-H(20B)	109.5	H(25A)-C(25)-H(25C)	109.5
C(16)-C(20)-H(20C)	109.5	H(25B)-C(25)-H(25C)	109.5
H(20A)-C(20)-H(20C)	109.5	B(1)-O(1)-C(17)	108.3(3)
H(20B)-C(20)-H(20C)	109.5	B(1)-O(2)-C(16)	107.6(3)
C(16)-C(21)-H(21A)	109.5	C(22)-O(4)-C(23)	117.2(4)
C(16)-C(21)-H(21B)	109.5	C(24)-O(6)-C(25)	116.3(4)

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for **61f**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$.

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
B(1)	52(2)	41(2)	54(2)	-7(2)	-6(2)	4(2)
C(1)	50(2)	35(2)	57(2)	5(2)	2(2)	0(2)
C(2)	50(2)	48(2)	64(2)	7(2)	0(2)	6(2)
C(3)	57(2)	44(2)	63(2)	4(2)	13(2)	9(2)
C(4)	62(2)	48(2)	61(2)	-4(2)	7(2)	8(2)
C(5)	50(2)	36(2)	56(2)	4(2)	6(2)	2(2)
C(6)	52(2)	43(2)	54(2)	-4(2)	1(2)	2(2)
C(7)	52(2)	46(2)	57(2)	3(2)	0(2)	-6(2)
C(8)	66(2)	64(3)	59(2)	-4(2)	-2(2)	-6(2)
C(9)	81(3)	102(4)	56(3)	-5(2)	-6(2)	-22(3)
C(10)	71(3)	105(4)	72(3)	17(3)	-22(2)	-16(3)
C(11)	58(2)	79(3)	92(3)	15(3)	-14(2)	-1(2)

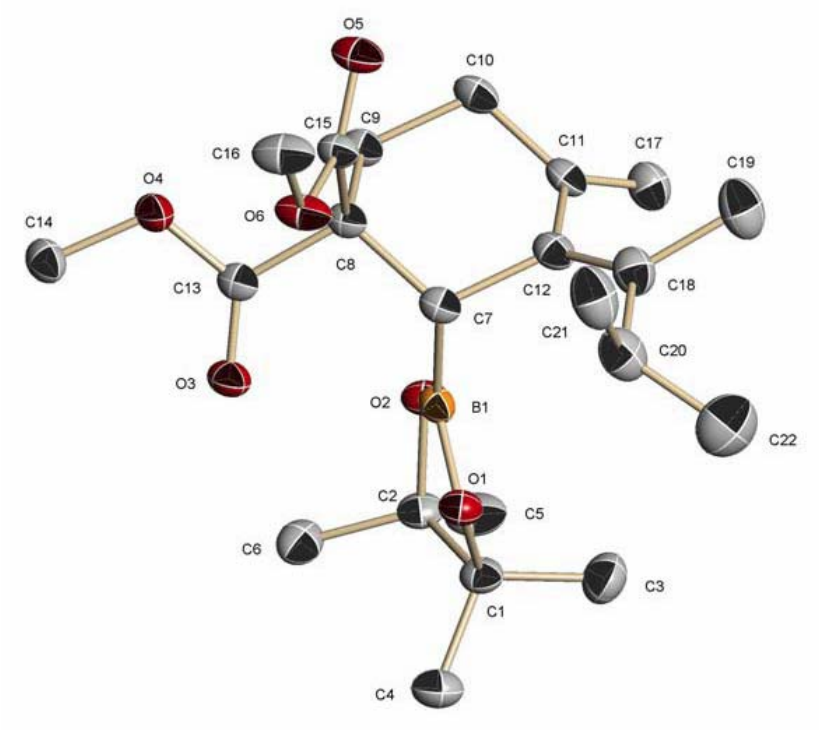
C(12)	51(2)	58(2)	74(3)	0(2)	-7(2)	-2(2)
C(13)	50(2)	45(2)	53(2)	-1(2)	-4(2)	3(2)
C(14)	78(3)	56(2)	55(2)	1(2)	7(2)	3(2)
C(15)	72(2)	62(3)	77(3)	1(2)	-24(2)	11(2)
C(16)	107(4)	43(3)	139(5)	16(3)	35(3)	19(2)
C(17)	76(3)	43(2)	104(4)	11(2)	16(3)	15(2)
C(18)	214(9)	116(6)	357(15)	116(8)	-204(10)	-52(6)
C(19)	347(13)	81(5)	230(9)	31(5)	183(10)	95(7)
C(20)	246(11)	107(6)	377(16)	140(9)	208(12)	90(7)
C(21)	201(9)	76(5)	580(30)	-77(9)	-215(13)	-3(5)
C(22)	69(3)	49(2)	80(3)	7(2)	21(2)	8(2)
C(23)	126(4)	65(3)	117(4)	35(3)	28(4)	42(3)
C(24)	69(3)	48(2)	79(3)	11(2)	15(2)	15(2)
C(25)	71(3)	130(5)	126(5)	41(4)	32(3)	-3(3)
O(1)	83(2)	50(2)	82(2)	12(1)	22(2)	23(1)
O(2)	75(2)	39(2)	106(2)	11(1)	28(2)	11(1)
O(3)	92(3)	66(2)	228(5)	50(3)	8(3)	-4(2)
O(4)	81(2)	61(2)	106(2)	30(2)	12(2)	24(2)
O(5)	114(3)	95(3)	90(2)	-13(2)	45(2)	2(2)
O(6)	62(2)	91(2)	94(2)	14(2)	16(2)	-8(2)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3) for **61f**.

	x	y	z	U(eq)
H(2)	3667	3709	3217	65
H(4A)	5809	4597	4218	69
H(4B)	5283	3878	4568	69
H(6)	7010	2711	3616	60
H(8)	7013	4018	4812	76
H(9)	8286	3943	5486	96
H(10)	9677	3001	5429	99
H(11)	9828	2163	4666	92
H(12)	8568	2233	3990	73
H(14A)	6102	3591	2465	95
H(14B)	6348	2687	2250	95
H(14C)	6932	3027	2772	95
H(15A)	3786	2365	2802	106
H(15B)	4518	2105	2310	106
H(15C)	4193	3045	2389	106
H(18A)	7607	136	3849	344
H(18B)	6893	872	4064	344
H(18C)	7832	1055	3657	344
H(19A)	6542	-139	2587	329

H(19B)	6840	-647	3114	329
H(19C)	7668	-25	2858	329
H(20A)	5527	270	4272	365
H(20B)	5366	-531	3911	365
H(20C)	4407	79	4015	365
H(21A)	4763	-553	3075	428
H(21B)	4939	217	2687	428
H(21C)	3971	206	3094	428
H(23A)	3430	6636	3661	154
H(23B)	2267	6383	3491	154
H(23C)	3209	6285	3073	154
H(25A)	2030	3096	4829	163
H(25B)	1225	3157	4339	163
H(25C)	1502	3957	4682	163

(*E*)-Dimethyl 3-(3-methylbutan-2-ylidene)-4-methylene-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclohexane-1,1-dicarboxylate (65c)



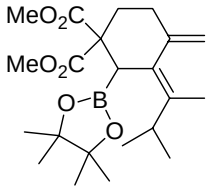


Table 1. Crystal data and structure refinement for **(*E*)-65c**.

Empirical formula	C22 H35 B O6
Formula weight	406.31

Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	Pca2(1)	
Unit cell dimensions	a = 13.7485(18) Å	α= 90°.
	b = 14.2046(19) Å	β= 90°.
	c = 12.0710(16) Å	γ = 90°.
Volume	2357.4(5) $Å^3$	
Z	4	
Density (calculated)	1.145 Mg/m^3	
Absorption coefficient	0.656 mm^{-1}	
F(000)	880	
Crystal size	0.18 x 0.10 x 0.04 mm^3	
Theta range for data collection	3.11 to 69.46°.	
Index ranges	-16<=h<=16, -16<=k<=16, -14<=l<=10	
Reflections collected	8710	
Independent reflections	3467 [R(int) = 0.0327]	
Completeness to theta = 69.46°	96.4 %	
Absorption correction	Semi-empirical from equivalents	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3467 / 1 / 402	
Goodness-of-fit on F^2	1.071	
Final R indices [I>2sigma(I)]	R1 = 0.0355, wR2 = 0.0916	
R indices (all data)	R1 = 0.0369, wR2 = 0.0930	
Absolute structure parameter	-0.06(15)	
Largest diff. peak and hole	0.318 and -0.170 e.$Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **(*E*)-65c**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
B(1)	9080(2)	7176(1)	1915(2)	22(1)
C(1)	7802(1)	7774(1)	2889(2)	26(1)
C(2)	8190(1)	6859(1)	3457(2)	27(1)
C(3)	8150(2)	8669(2)	3444(2)	40(1)
C(4)	6716(2)	7799(2)	2718(2)	34(1)
C(5)	8358(2)	6942(2)	4700(2)	39(1)
C(6)	7571(2)	5998(1)	3192(2)	35(1)
C(7)	9894(1)	7200(1)	991(2)	22(1)

C(8)	10332(1)	6230(1)	682(2)	21(1)
C(9)	11016(1)	5843(1)	1582(2)	24(1)
C(10)	11801(1)	6560(1)	1913(2)	27(1)
C(11)	11372(1)	7508(1)	2185(2)	25(1)
C(12)	10689(1)	7901(1)	1352(2)	25(1)
C(13)	9495(1)	5531(1)	516(2)	23(1)
C(14)	9095(2)	4043(1)	-231(2)	29(1)
C(15)	10854(1)	6303(1)	-433(2)	23(1)
C(16)	10605(2)	6468(2)	-2350(2)	38(1)
C(17)	11567(2)	7943(2)	3138(2)	33(1)
C(18)	10735(2)	8786(1)	964(2)	32(1)
C(19)	11579(2)	9436(2)	1237(2)	45(1)
C(20)	9977(2)	9201(2)	183(2)	39(1)
C(21)	10332(2)	9171(2)	-1016(2)	45(1)
C(22)	9689(3)	10207(2)	534(3)	56(1)
O(1)	8275(1)	7738(1)	1808(1)	24(1)
O(2)	9134(1)	6725(1)	2912(1)	25(1)
O(3)	8663(1)	5671(1)	767(1)	28(1)
O(4)	9822(1)	4740(1)	58(1)	28(1)
O(5)	11712(1)	6228(1)	-591(1)	31(1)
O(6)	10208(1)	6459(1)	-1248(1)	31(1)

Table 3. Bond lengths [Å] and angles [°] for **(*E*)-65c**.

B(1)-O(2)	1.365(3)	C(6)-H(6B)	1.02(3)
B(1)-O(1)	1.371(2)	C(6)-H(6C)	1.04(3)
B(1)-C(7)	1.580(3)	C(7)-C(12)	1.542(2)
C(1)-O(1)	1.459(2)	C(7)-C(8)	1.549(2)
C(1)-C(4)	1.509(3)	C(7)-H(7)	0.98(2)
C(1)-C(3)	1.514(3)	C(8)-C(15)	1.529(3)
C(1)-C(2)	1.564(3)	C(8)-C(13)	1.534(2)
C(2)-O(2)	1.467(2)	C(8)-C(9)	1.539(2)
C(2)-C(5)	1.523(3)	C(9)-C(10)	1.537(2)
C(2)-C(6)	1.524(3)	C(9)-H(9A)	1.02(2)
C(3)-H(3A)	1.01(3)	C(9)-H(9B)	0.97(2)
C(3)-H(3B)	0.93(3)	C(10)-C(11)	1.507(3)
C(3)-H(3C)	1.01(3)	C(10)-H(10A)	1.00(3)
C(4)-H(4A)	1.02(3)	C(10)-H(10B)	0.98(2)
C(4)-H(4B)	0.96(3)	C(11)-C(17)	1.334(3)
C(4)-H(4C)	0.97(3)	C(11)-C(12)	1.485(3)
C(5)-H(5A)	0.98(3)	C(12)-C(18)	1.342(3)
C(5)-H(5B)	0.98(3)	C(13)-O(3)	1.200(2)
C(5)-H(5C)	0.99(3)	C(13)-O(4)	1.330(2)
C(6)-H(6A)	0.97(3)	C(14)-O(4)	1.449(2)

C(14)-H(14A)	0.96(3)	C(1)-C(4)-H(4A)	110.3(17)
C(14)-H(14B)	0.99(3)	C(1)-C(4)-H(4B)	109.4(17)
C(14)-H(14C)	0.94(3)	H(4A)-C(4)-H(4B)	111(2)
C(15)-O(5)	1.200(2)	C(1)-C(4)-H(4C)	109.4(13)
C(15)-O(6)	1.344(2)	H(4A)-C(4)-H(4C)	109(2)
C(16)-O(6)	1.439(2)	H(4B)-C(4)-H(4C)	107(2)
C(16)-H(16A)	1.01(3)	C(2)-C(5)-H(5A)	112.9(18)
C(16)-H(16B)	0.93(3)	C(2)-C(5)-H(5B)	110.7(16)
C(16)-H(16C)	0.94(3)	H(5A)-C(5)-H(5B)	109(2)
C(17)-H(17A)	0.94(3)	C(2)-C(5)-H(5C)	109.3(16)
C(17)-H(17B)	0.96(3)	H(5A)-C(5)-H(5C)	110(2)
C(18)-C(19)	1.520(3)	H(5B)-C(5)-H(5C)	104(2)
C(18)-C(20)	1.524(3)	C(2)-C(6)-H(6A)	108.2(16)
C(19)-H(19A)	0.99(3)	C(2)-C(6)-H(6B)	111.4(15)
C(19)-H(19B)	0.95(4)	H(6A)-C(6)-H(6B)	107(2)
C(19)-H(19C)	0.95(3)	C(2)-C(6)-H(6C)	111.6(13)
C(20)-C(21)	1.528(4)	H(6A)-C(6)-H(6C)	112(2)
C(20)-C(22)	1.541(4)	H(6B)-C(6)-H(6C)	107(2)
C(20)-H(20)	0.97(3)	C(12)-C(7)-C(8)	111.52(14)
C(21)-H(21A)	1.01(3)	C(12)-C(7)-B(1)	108.43(15)
C(21)-H(21B)	1.00(3)	C(8)-C(7)-B(1)	115.23(14)
C(21)-H(21C)	0.91(3)	C(12)-C(7)-H(7)	111.0(13)
C(22)-H(22A)	0.97(3)	C(8)-C(7)-H(7)	104.4(13)
C(22)-H(22B)	0.98(4)	B(1)-C(7)-H(7)	106.1(13)
C(22)-H(22C)	0.91(4)	C(15)-C(8)-C(13)	106.37(14)
O(2)-B(1)-O(1)	113.62(17)	C(15)-C(8)-C(9)	111.04(14)
O(2)-B(1)-C(7)	126.43(16)	C(13)-C(8)-C(9)	108.62(14)
O(1)-B(1)-C(7)	119.49(16)	C(15)-C(8)-C(7)	109.52(14)
O(1)-C(1)-C(4)	108.66(17)	C(13)-C(8)-C(7)	108.38(14)
O(1)-C(1)-C(3)	106.56(16)	C(9)-C(8)-C(7)	112.67(15)
C(4)-C(1)-C(3)	110.70(17)	C(10)-C(9)-C(8)	112.09(15)
O(1)-C(1)-C(2)	102.16(13)	C(10)-C(9)-H(9A)	109.5(14)
C(4)-C(1)-C(2)	114.70(16)	C(8)-C(9)-H(9A)	107.5(14)
C(3)-C(1)-C(2)	113.30(18)	C(10)-C(9)-H(9B)	109.1(13)
O(2)-C(2)-C(5)	108.54(16)	C(8)-C(9)-H(9B)	107.0(13)
O(2)-C(2)-C(6)	107.21(15)	H(9A)-C(9)-H(9B)	111.7(18)
C(5)-C(2)-C(6)	110.71(19)	C(11)-C(10)-C(9)	112.00(15)
O(2)-C(2)-C(1)	102.31(14)	C(11)-C(10)-H(10A)	111.0(14)
C(5)-C(2)-C(1)	114.80(17)	C(9)-C(10)-H(10A)	108.0(13)
C(6)-C(2)-C(1)	112.60(17)	C(11)-C(10)-H(10B)	108.3(13)
C(1)-C(3)-H(3A)	106.9(15)	C(9)-C(10)-H(10B)	108.3(13)
C(1)-C(3)-H(3B)	112.0(18)	H(10A)-C(10)-H(10B)	109.1(19)
H(3A)-C(3)-H(3B)	109(2)	C(17)-C(11)-C(12)	122.52(18)
C(1)-C(3)-H(3C)	109.9(17)	C(17)-C(11)-C(10)	121.55(19)
H(3A)-C(3)-H(3C)	115(2)	C(12)-C(11)-C(10)	115.86(17)
H(3B)-C(3)-H(3C)	104(2)	C(18)-C(12)-C(11)	123.92(18)

C(18)-C(12)-C(7)	122.65(18)	C(18)-C(19)-H(19B)	109.3(19)
C(11)-C(12)-C(7)	113.41(15)	H(19A)-C(19)-H(19B)	116(3)
O(3)-C(13)-O(4)	124.51(16)	C(18)-C(19)-H(19C)	110.6(17)
O(3)-C(13)-C(8)	125.15(16)	H(19A)-C(19)-H(19C)	108(3)
O(4)-C(13)-C(8)	110.34(15)	H(19B)-C(19)-H(19C)	101(3)
O(4)-C(14)-H(14A)	107.9(15)	C(18)-C(20)-C(21)	110.9(2)
O(4)-C(14)-H(14B)	106.1(14)	C(18)-C(20)-C(22)	111.4(2)
H(14A)-C(14)-H(14B)	118(2)	C(21)-C(20)-C(22)	111.6(2)
O(4)-C(14)-H(14C)	111.5(14)	C(18)-C(20)-H(20)	106.5(15)
H(14A)-C(14)-H(14C)	108(2)	C(21)-C(20)-H(20)	108.7(15)
H(14B)-C(14)-H(14C)	106(2)	C(22)-C(20)-H(20)	107.5(15)
O(5)-C(15)-O(6)	123.26(18)	C(20)-C(21)-H(21A)	108.6(19)
O(5)-C(15)-C(8)	126.57(17)	C(20)-C(21)-H(21B)	107.7(18)
O(6)-C(15)-C(8)	110.16(14)	H(21A)-C(21)-H(21B)	114(3)
O(6)-C(16)-H(16A)	109.5(18)	C(20)-C(21)-H(21C)	111.5(16)
O(6)-C(16)-H(16B)	113.6(19)	H(21A)-C(21)-H(21C)	107(2)
H(16A)-C(16)-H(16B)	106(3)	H(21B)-C(21)-H(21C)	108(2)
O(6)-C(16)-H(16C)	105.1(17)	C(20)-C(22)-H(22A)	111.3(19)
H(16A)-C(16)-H(16C)	110(2)	C(20)-C(22)-H(22B)	106(2)
H(16B)-C(16)-H(16C)	113(2)	H(22A)-C(22)-H(22B)	108(3)
C(11)-C(17)-H(17A)	118.8(14)	C(20)-C(22)-H(22C)	111(2)
C(11)-C(17)-H(17B)	119.9(18)	H(22A)-C(22)-H(22C)	104(3)
H(17A)-C(17)-H(17B)	121(2)	H(22B)-C(22)-H(22C)	117(3)
C(12)-C(18)-C(19)	122.0(2)	B(1)-O(1)-C(1)	107.22(14)
C(12)-C(18)-C(20)	123.12(19)	B(1)-O(2)-C(2)	106.63(14)
C(19)-C(18)-C(20)	114.86(18)	C(13)-O(4)-C(14)	116.37(14)
C(18)-C(19)-H(19A)	111.4(17)	C(15)-O(6)-C(16)	115.32(14)

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for **(*E*)-65c**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$.

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
B(1)	21(1)	26(1)	20(1)	-2(1)	0(1)	-3(1)
C(1)	24(1)	31(1)	23(1)	-1(1)	6(1)	2(1)
C(2)	24(1)	33(1)	24(1)	1(1)	7(1)	3(1)
C(3)	46(1)	33(1)	41(1)	-8(1)	5(1)	0(1)
C(4)	26(1)	40(1)	36(1)	3(1)	5(1)	4(1)
C(5)	36(1)	59(1)	22(1)	1(1)	6(1)	11(1)
C(6)	37(1)	31(1)	36(1)	3(1)	14(1)	-1(1)
C(7)	21(1)	29(1)	18(1)	3(1)	-1(1)	0(1)
C(8)	20(1)	29(1)	16(1)	0(1)	-1(1)	1(1)

C(9)	22(1)	30(1)	20(1)	2(1)	-3(1)	0(1)
C(10)	19(1)	37(1)	24(1)	2(1)	-5(1)	-2(1)
C(11)	19(1)	32(1)	25(1)	2(1)	0(1)	-6(1)
C(12)	22(1)	33(1)	21(1)	0(1)	4(1)	-3(1)
C(13)	22(1)	31(1)	14(1)	0(1)	-1(1)	0(1)
C(14)	29(1)	34(1)	26(1)	-4(1)	0(1)	-5(1)
C(15)	19(1)	29(1)	21(1)	0(1)	-1(1)	1(1)
C(16)	30(1)	64(1)	19(1)	2(1)	2(1)	10(1)
C(17)	34(1)	36(1)	30(1)	-1(1)	-5(1)	-5(1)
C(18)	35(1)	32(1)	30(1)	1(1)	2(1)	-6(1)
C(19)	51(1)	38(1)	47(2)	8(1)	-5(1)	-15(1)
C(20)	40(1)	33(1)	43(1)	15(1)	-5(1)	-7(1)
C(21)	55(2)	40(1)	41(1)	10(1)	-9(1)	-15(1)
C(22)	67(2)	45(1)	55(2)	14(1)	-4(2)	8(1)
O(1)	21(1)	30(1)	22(1)	3(1)	3(1)	1(1)
O(2)	22(1)	34(1)	20(1)	2(1)	4(1)	4(1)
O(3)	21(1)	36(1)	27(1)	-5(1)	4(1)	-1(1)
O(4)	23(1)	32(1)	30(1)	-9(1)	1(1)	-2(1)
O(5)	20(1)	49(1)	24(1)	-1(1)	2(1)	1(1)
O(6)	21(1)	55(1)	17(1)	2(1)	1(1)	5(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3) for **(*E*)-65c**.

	x	y	z	U(eq)
H(3A)	7780(20)	8723(17)	4170(30)	41(7)
H(3B)	8020(19)	9200(20)	3020(30)	43(7)
H(3C)	8880(20)	8660(20)	3510(30)	48(7)
H(4A)	6370(20)	7750(20)	3460(30)	51(8)
H(4B)	6540(20)	8370(20)	2340(30)	44(7)
H(4C)	6521(17)	7273(16)	2250(20)	25(5)
H(5A)	8620(20)	6360(20)	5030(30)	46(7)
H(5B)	7750(20)	7120(18)	5080(20)	43(7)
H(5C)	8807(18)	7471(17)	4850(20)	30(6)
H(6A)	7920(20)	5444(19)	3440(20)	40(7)
H(6B)	7480(20)	5921(17)	2360(20)	36(6)
H(6C)	6881(18)	6046(17)	3550(20)	31(6)
H(7)	9572(16)	7412(15)	310(20)	23(5)
H(9A)	11339(18)	5253(17)	1270(20)	31(6)
H(9B)	10615(16)	5701(15)	2230(20)	23(5)
H(10A)	12163(17)	6299(16)	2560(20)	28(6)
H(10B)	12248(17)	6636(15)	1290(20)	26(5)
H(14A)	8820(18)	3803(17)	450(20)	33(6)
H(14B)	9421(17)	3592(17)	-730(20)	32(6)

H(14C)	8584(18)	4310(16)	-650(20)	31(6)
H(16A)	11050(20)	7020(20)	-2430(30)	53(8)
H(16B)	10970(20)	5940(20)	-2520(30)	48(8)
H(16C)	10070(20)	6540(18)	-2820(20)	37(6)
H(17A)	11996(19)	7655(16)	3640(20)	27(6)
H(17B)	11279(19)	8547(19)	3290(20)	39(6)
H(19A)	12130(20)	9090(20)	1560(30)	51(8)
H(19B)	11730(20)	9810(20)	610(30)	55(8)
H(19C)	11380(20)	9900(20)	1750(30)	44(7)
H(20)	9401(19)	8808(17)	250(20)	34(6)
H(21A)	10980(20)	9500(20)	-1060(30)	52(8)
H(21B)	9820(20)	9460(20)	-1490(30)	56(8)
H(21C)	10427(18)	8570(19)	-1250(20)	33(6)
H(22A)	9500(20)	10230(20)	1310(30)	53(8)
H(22B)	9120(30)	10370(30)	80(30)	68(10)
H(22C)	10210(30)	10600(20)	490(30)	62(10)